SERUM AMINOTRANSFERASE LEVELS IN THE ASSESSMENT OF SEVERITY OF DENGUE FEVER

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations

for the award of the degree of

M.D. GENERAL MEDICINE (BRANCH - I)

INSTITUTE OF INTERNAL MEDICINE

MADRAS MEDICAL COLLEGE

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THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2014

CERTIFICATE

This is to certify that the dissertation titled **"SERUM AMINOTRANSFERASE LEVELS IN THE ASSESSMENT OF SEVERITY OF DENGUE FEVER"** is the bonafide original work of **Dr.B.GOVINDARAJAN** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in APRIL 2014. The Period of study was from June 2013 to November 2013.

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DECLARATION

I, **Dr.B.GOVINDARAJAN** solemnly declare that dissertation titled **"Serum Aminotransferase levels in the Assessment of severity of Dengue Fever"** is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during June 2013 to November 2013 under the guidance and supervision of my unit chief **Prof. K.Sivasubramanian, M.D.,** Director and Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine – April 2014.**

Place : Chennai **(Dr. B.GOVINDARAJAN)**

Date :

ACKNOWLEDGEMENT

I owe my thanks to the Dean, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 **Dr. V.KANAGASABAI, M.D., MBA** for allowing me to avail the facilities needed for my dissertation work.

I am grateful to beloved mentor **Prof.Dr.K.SIVASUBRAMANIAN, M.D.,** Director and Professor, Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai for permitting me to do the study and for her encouragement.

I am extremely thankful to my Assistant Professors **Dr.M.Anusuya, M.D.,** and **Dr.D.K.Sivakumar** for their guidance and encouragement.

I am also thankful to all my unit colleagues for their full cooperation in this study and my sincere thanks to all the patients and their families who co-operated for this study.

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ABSTRACT

INTRODUCTION

Dengue fever is highly prevalent in Tamilnadu and it has caused several outbreaks in the recent years .Notable areas involved in the recent outbreaks includes Chennai, Madurai and Tirunelveli with significant mortality and morbidity. Most patients with dengue fever have liver involvement in the form of elevated serum aminotransferases. The elevation of enzymes is due to reactive hepatitis as well as direct injury to hepatocytes by the virus itself. Patients with hepatitis are more likely to have increased risk of bleeding tendencies, renal failure, encephalopathy and acalculous cholecystitis. In addition to thrombocytopenia, deranged liver function plays a significant role in bleeding. Hence, evaluation of liver function, particularly the aminotransferases, should be a routine in the management of dengue fever.

METHODS

A total of 60 patients with dengue IG-M ELISA positive admitted to Institute of Internal Medicine, Rajiv Gandhi Government General Hospital, Chennai were included in this study. Patients have their history taken according to a questionnaire and subjected to clinical examination and investigations like complete blood count, plasma glucose, blood urea, serum creatinine, QBC for MP/MF, MSAT for leptospirosis, blood culture, widal

test, anti-HAV, HBsAg, anti HCV, chest X- ray, USG abdomen and liver function tests.

RESULTS

Out of 60 patients, 36 patients had elevated liver enzymes. Those patients were at risk of severe bleeding, shock, ARDS, hepatitis and other complications. There was a significant difference (p value<0.05) between serum aminotransferase values and bleeding, shock, ARDS and hepatitis. There was a negative correlation between liver enzymes and platelets. Of the liver enzymes, AST levels were higher compared to ALT levels (mean AST-259.45& mean ALT- 199.75).

CONCLUSION

Hepatic involvement is common in dengue fever. It is characterised by elevated liver enzymes, AST more than ALT levels. Elevated liver enzymes were associated with complications like bleeding, shock and organ impairment. In addition to thrombocytopenia, hepatic involvement plays a significant role in bleeding. Elevated liver enzymes have got prognostic value in this study. Hence, liver enzymes are mandatory in dengue fever to look for complications and it is of prognostic value. Those patients with elevated liver enzymes should be monitored carefully than those with normal liver enzymes.

Key Words:
Dengue Fever, Serum Aminotransferases, Thrombocytopaenia, Bleeding.

INTRODUCTION

Dengue fever (DF) is usually a self limited mosquito borne viral disease.It is caused by one among the 4 subtypes of dengue viruses. Characteristic features are fever and minimal constitutional symptoms to shock and bleeding tendencies or dengue shock syndrome / dengue hemorrhagic fever (DSS/DHF). The worldwide spread of dengue has increased dramatically nowadays to be endemic in 112 countries of South East Asia, Africa, South and North America and the Mediterranean regions. In tropical and subtropical regions nearly about 2.5 billion people are at risk for dengue fever.

Each year around 45-105 million reported cases of dengue, 550,000 reported cases of dengue hemorrhagic fever & atleast about 13,000 deaths because of dengue occurs throughout the world. 90% of dengue mortality was seen in children <14 years. Dengue fever and dengue hemorrhagic fever is currently endemic in countries like Bangladesh, Myanmar, Sri Lanka, India, Thailand and other South East Asian countries.

Dengue fever is highly prevalent in Tamilnadu and it has caused several outbreaks in the recent years. Notable areas involved in the recent

outbreaks include Chennai, Tirunelveli and Madurai with significant morbidity and mortality.

The spectrum of dengue fever includes:

- Asymptomatic
- Acute Fever
- Classical dengue
- 'Dengue hemorrhagic fever' including the 'Dengue shock syndrome'.

'Classical Dengue' fever evolves through three phases:

- Febrile phase
- Critical phase
- Recovery phase

Though dengue is a self limited viral disease, it leads to life threatening complications in significant number of patients especially during the critical phase of the illness.

'Severe dengue' is classified by the following characteristics:

- Plasma leakage causing shock, the dengue shock & free fluid accumulation along with respiratory suffocation or without it.
- Massive bleeding
- Severe organ damage

The standard of care in the management of dengue fever involves close monitoring of vital parameters, platelet count and hematocrit. It has been shown that most patients with dengue fever have liver involvement in the form of elevated serum aminotransferases. The elevation of enzymes is due to reactive hepatitis as well as direct injury to hepatocytes by the virus itself. Patients with hepatitis are more likely to have increased risk of bleeding tendencies, renal failure, encephalopathy and acalculous cholecystitis. In addition to thrombocytopenia, deranged liver function plays a significant role in bleeding. Hence, evaluation of liver function, particularly the aminotransferases, should be a routine in the management of patients with dengue fever.

AIMS AND OBJECTIVES

PRIMARY OBJECTIVE

- *To measure serum aminotransferase levels in patient with dengue fever*

SECONDARY OBJECTIVE

- To correlate serum aminotransferase levels with the severity of dengue fever

REVIEW OF LITERATURE

The term "Dengue" was introduced from the West Indies into the English medical literature during the year 1827 – 28, Caribbean epidemic of an exanthema with arthralgia. It is a Spanish homonym for the Swahili "Ki denga Pepo" which is a sudden cramp like seizure caused due to an evil spirit. The usage of the term "Break bone fever" for the dengue was known since 1780 in Philadelphia.

In 1897, numerous shock cases and deaths were reported due to dengue epidemic in queensland,Australia. Similar incident was noted during the massive dengue epidemic of 1928 which occurred in greek where nearly 1250 persons died because of dengue. The greek epidemic was due to the poor living conditions among refugees from Turkey following the 1922 Greco-Turkish war . The dengue viruses were adapted to laboratory animals for the first time during 1940's (type land 2) and 1950's (type 3 and 4)[6,7].

INCIDENCE

Global burden

"Dengue Hemorrhagic fever (DHF)" is defined by 4 major features viz.

- High grade Fever
- Bleeding phenomena

- Liver enlargement
- Signs of circulatory failure

Dengue outbreaks were noticed over the 19th & early part of 20th centuries. Notable areas include the "Southern part of Europe, America, Northern part of Africa, Asia and Australia, the eastern part of Mediterranean and on numerous islands in the Arabian Ocean & the Caribbean"[1,2].

Dengue in the South-East Regions of Asia & Western part of Pacific Regions

'Dengue hemorrhagic fever' was first noticed in 1953 in Philippines. It was linked to dengue viruses etiologically because of dengue subtypes two, three and four recovered from patients in 1956.Numerous subtypes of dengue viruses were discovered from patients in Thailand two years later in an epidemic. After thirty years, DHF/DSS was found in some parts of "china, Malaysia, Cambodia, Malaysia, the Republic of Lao people and several pacific island groups"[1,2].

" Dengue haemorrhagic fever/Dengue shock syndrome" progressively spreading as an major public health concern, from its prime location to small towns & cities in epidemic areas during 1960s and 1970s. It followed a seasonal and also a periodical outbreak patterns, with epidemics occurring regularly at two or three years gap. In 1980s, "DHF/DSS" affected even the

smaller villages in the endemic countries. Exceptionally larger outbreaks happened in Vietnam and Thailand in 1988.The amount of people acquiring & dying due to 'DHF/DSS' noticed in every parts of south east Asia & western pacific was 23,793 and 1,946,965 respectively during 1980s. New introductions of DHF/DSS were reported in India (1988), New Caledonia (1988), China (1985), Srilanka (1989), Tahiti (1989), and Maldives (1985) epidemiologically. The reports in Sri Lanka and India are interesting particularly because 'virological surveillance in these areas reported the local transmission of four dengue serotypes and DF cases, but not due to'DHF/DSS' previous to the above mentioned massive outbreaks'[1,2].

The sequence has been the same in each of these countries where DHF has becoming endemic. Frequent dengue virus transmission, initially due to single cases of 'Dengue haemorrhagic fever' and then succeeded by DHF outbreaks were increasing gradually until the DHF cases were seen almost all the year, with severe outbreaks taking place at an interval of 3 to 5 years. All 4 dengue virus serotypes are seen in these two regions, and because of increasing international travelers, new virus serotypes and strains were rapidly introduced into the susceptible populations. 'Dengue fever and Dengue haemorrhagic fever', primarily an disease affecting young children because of the largest proportion of susceptible individuals within the group of population at risk for disease. Interestingly, among the travelers,

DF & DHF is now occasionally found. Dengue haemorrhagic feve is causing an severe public health related problems in many regions in the South-East part of Asian countries and also in some Pacific regions. 'One of the 10 major reasons for hospitalization and mortality in younger age groups in about 8 countries in Asia is due to dengue'[1,2].

Epidemics of the dengue illness in India[8]

Dengue fever is endemic in most parts of our country in exception to the Himalayan and other hilly regions where conditions are not suitable for the vector to propogate.

In some countries there is an periodical pattern of virus spread especially during the winter season "Temperature & Rain" are the two most significant factors for dengue virus spread, since decreased temperatures will affect the survival of adult mosquitoes and thereby affecting the transmission rates. In addition to, rain & temperature also alter the mosquito pattern of reproduction and also feeding, and thereby affecting the population density of vectors.

Though DHF may affect persons of all age groups, most of the cases are seen in children of < 14 years of age in endemic areas. The local trend in Bangkok, Thailand since 1964 has progressively approaching the lesser

attack ratio, with the modal age for in hospital child being six to seven years all over the Thailand. A modest increase of affected girls compared to boys in some areas whereas other regions have almost showed an even gender distribution in surveillance data.

DENGUE VIRUSES

Dengue fever is due to dengue virus belonging to the genus "flavivirus" and the family "flaviviridae". It is composed of a single standard RNA virus of four distinct serotypes '(DEN I to IV)'. Dengue virus is 50 mm in diameter and it is spherical in shape. It contains "multiple copies of the three structural proteins, a copy of a positive sense, single stranded RNA genome and a host derived membrane bilayer". It also contains seven nonstructural proteins (NS). The biologically important viral properties are situated in the E protein. Some of the 'nonstructural proteins are important in the viral replication'[9]. Individuals infected with one dengue virus subtype are immune to that subtype only. Theoretically, all four dengue subtypes can infect the individuals. Initially DEN-2 was the predominant serotype but now DEN-3 has becoming more common[10].

Transmission

It is spread to human beings mainly through the bites of infected 'Aedes mosquitoes', mostly "Aedes aegypti". Other species responsible for transmission to humans are "Aedes albopictus, Aedes polynesiensis and

several species of the Aedes scrotellaris complex". The female mosquitoes are incorporated with dengue virus after they suck bloody meal from the diseased person at the time of fever (viraemic phase).The infected mosquitoes then transmit the infection by biting as well as injecting infected salivary fluid in to other person after an extrinsic incubation period of about eight to ten days. A single female mosquito which is infected is adequate for vertical transmission of the virus to following generation, which is responsible for the virus maintenance and not for the epidemiology aspect of the disease. Rarely a mother to child transmission was also reported.

Transmission of dengue virus occurs in variable areas, including tropical and subtropical areas at different altitudes. The Aedes rests mainly in indoors, in bedrooms and in living rooms and also in small water collections like coconut shells and flowerpots[11,12]. This increases man to vector contact and thereby reducing the mosquitoes contact with insecticidal agents sprayed outsides and thereby hindering the control of the vectors[13]. Mosquito eggs are able to survive for longer duration of time. In endemic areas, high mosquito densities are due to the improper garbage disposal and inadequate waste water drainage system. There is a 'significant improvement in the larval productions of the mosquito during rainy season

and that is the reason for outbreaks of dengue occurring during rainy season'.

Pathogenesis

The average incubation period lasts for about 3 to 8 days (range of 4to 15 days) after the infected mosquitoes bites the human beings. Depending on the characteristics of the viruses, the diseased individuals may or may not be able to experience symptoms.' The incubation period is immediately followed by viremia, characterized by sudden occurence of fever and systemic symptoms seen for about 5 to 8 days (range of 2 to 13 days)'.

Replication of dengue virus occurs inside the cellular matter of the macrophages, B cells & monocytes. In addition," mast cells[14], dendritic cells &endothelial cells" are also infected with dengue virus. It may also infect "liver, spleen, peripheral blood WBCs, lymph nodes, thymus, kidney, cardiac, lungs, stomach, and possibly the human brain", which suggest disruption of blood brain barrier[15].

The viremic phase is followed by either dengue and dengue hemorrhagic fever. After that the patient will either recover from the illness or they may advances to the more severe leakage syndrome, the Dengue shock syndrome. The dengue infections severity are correlated with the

presence of peak plasma viremia and circulating levels of NS1 protein[16]. There is an increased expression of cytokines mainly 'Tumour necrosis factor-α and Interferon- α'[17,18], and also other chemical substances when the number of infected cells are more. These cytokines in turn leads to the over expression of another dendritic cells either infected or non-infected with viruses. The expression of numerous cytokines and other chemical mediators are important for the "excessive plasma leakage, decreased effective circulating volume, increased vascular permeability, coagulation abnormalities and shock". Additionally, it is found that an supportive evidence for apoptosis of endothelial cells leading to disintegration of the endothelial cell barrier and thereby causing the generalized vascular leak syndrome[19].

In about 2 to 4% of individuals, there was a more serious infection, when a person was infected with a different serotype for a second time. The reason for second time dengue infection causing an serious illness and why only small amount of the patients are severely diseased still remains mysterious.

Commonly occurring gross pathologic findings like "petechial hemorrhages and purpurae, serous effusions, & also pulmonary congestion". Small vessel vasculitis is seen in visceral and soft tissues on

microscopy and there were some amount of "focal middle zone liver necrosis,gastric mucosal bleeding & subendocardial left ventricle bleeding".

The remaining antibodies synthesized early in the initial infection are not able to antogonise an another infection with a different serotype. The second time infection results in severe disease due to the influence of enhancing antibodies. This phenomenon is called as "Antibody –dependent enhancement"[20].

CLINICAL FEATURES

Dengue fever has got a numerous spectrum of clinical features. Mostly with unexplained cause and outcome. It is mostly a self relieving less severe disease but a small population of dengue fever progresses to severe disease due to plasma leakage with or without hemorrhage.

Symptomatic dengue infections were classified in to three groups[21,22]

1. Undifferentiated fever
2. Dengue Fever (DF)
3. Dengue hemorrhagic fever (DHF) – four grades. Grade III and IV Dengue Hemorrhagic Fever (DHF) are called as Dengue Shock Syndrome(DSS).

Probable Dengue

Live in/travel to dengue occurring area

"Fever plus any two of the following features:

- Nausea, vomiting
- Exanthematous rash
- Muscle aches & pains
- Positive for tourniquet procedure
- Reduced leucocyte count
- Any of the warning signs"

"Warning signs of dengue are:

- Epigastric pain or tenderness
- Prolonged vomiting
- Clinically accumulation of fluid
- Mucosal haemorrhages
- Slowness, restlessness
- Hepatic enlargement greater than 2 cm
- Increased HCT concurrent with rapid fall in thrombocytes count".

"Severe Dengue Criteria[21,22]

1. Severe leakage of plasma causing
    a. Shock (DSS)
    b. Respiratory suffocation
2. Massive bleeding

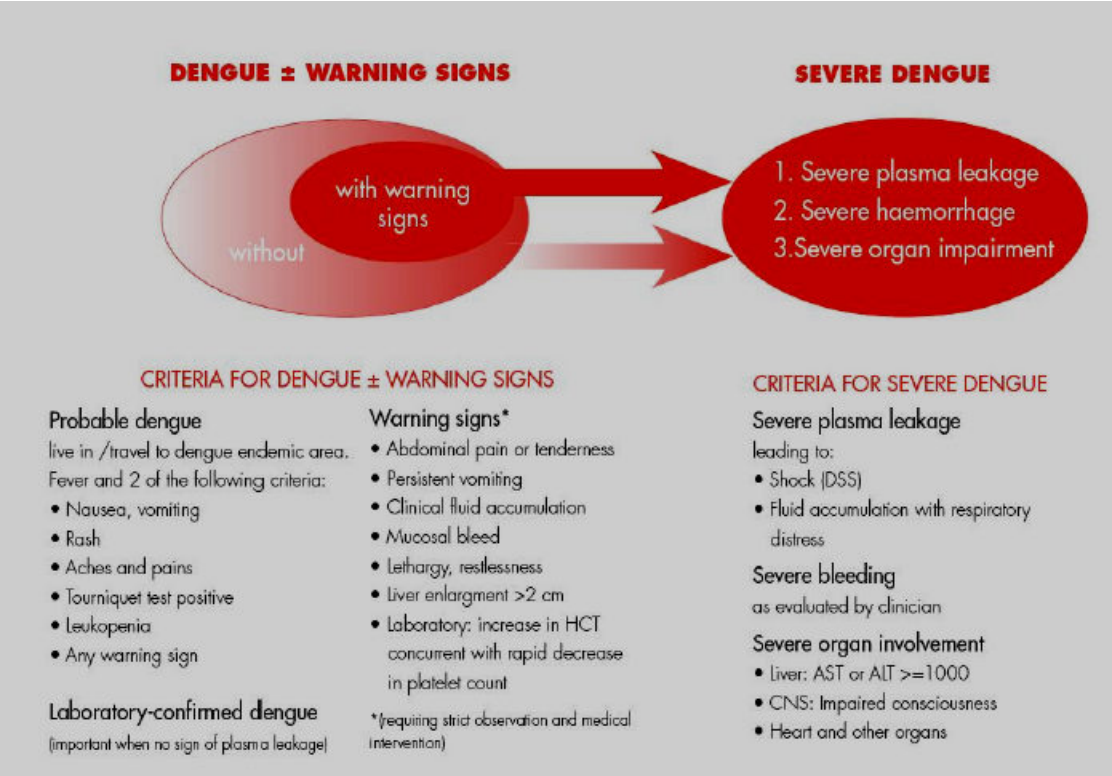
3. Severe damage to internal organs

    a. Liver : AST and ALT more than 1000

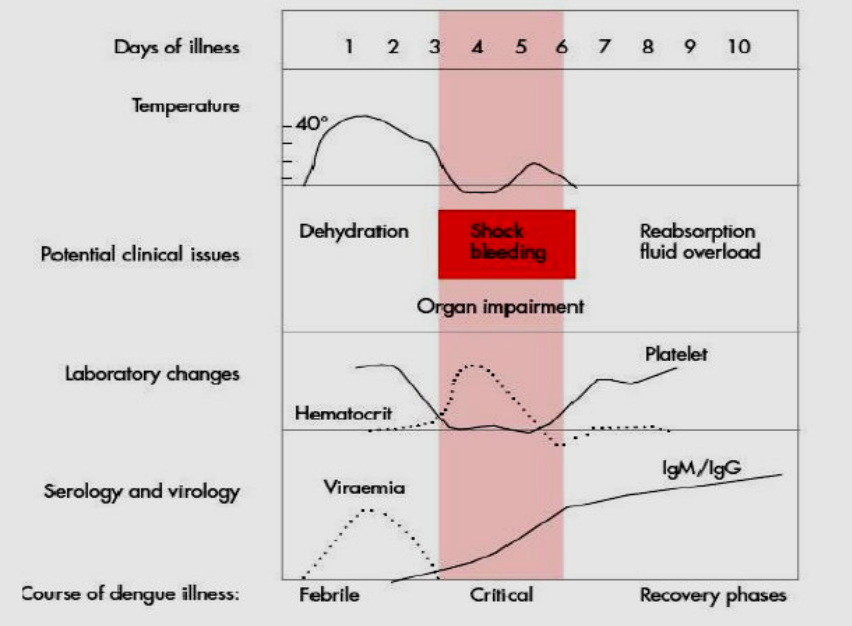
    b. CNS : altered sensorium

    c. cardiac & other internal organs”

DENGUE - CLASSIFICATION OF CASES & LEVELS IN THE SEVERITY OF ILLNESS



DENGUE FEVER - COURSE OF ILLNESS



"3 phases of Dengue Fever:

- Febrile phase
- Critical phase
- Recovery phase"

Febrile Phase

- Lasts for 3 – 8 days
- Clinically it resembles like any other febrile diseases

  Characterized by body ache, headache, arthralgia, sore throat, etc.,
- Clinical presentations are indistinguishable in between severe and mild dengue.

- ❖ Minimal bleeding manifestations may be seen.
- ❖ Earliest abnormality is a 'progressive reduction in total white blood cell count, which may alert the treating doctor to suspect a high probability of dengue'.

Critical phase

- ❖ Increase in capillary permeability as evidenced by increasing haematocrit levels at the time of defervescence.
- ❖ Significant plasma leakage lasts for 24 – 48 hours
- ❖ Before plasma leakage, there is a progressive leucopenia followed by rapid decrease in thrombocytes.
- ❖ Shock occurs in this phase which is preceded by warning signs.
- ❖ Progressive organ impairment, metabolic acidosis and DIC occurs because of prolonged shock.
- ❖ Total wbc count may rise in patients with massive bleeding.
- ❖ Severe hepatic involvement, meningoencephalitis, myocarditis and profuse bleeding may occur even in the absence of obvious leakage of plasma and shock.

Recovery phase

Following 24 – 48 hours of critical phase, there will be a gradual absorption of extravascular compartment fluid. General condition of the patient and hemodynamic status improves. Bradycardia and other ECG

changes are common. WBC returns to normal after that platelet count becomes normal. Excessive fluid management in this phase is associated with pulmonary odema or congestive cardiac failure.

Hemodynamic Assessment

Parameters	Stable circulation	Compensated shock	Hypotensive shock
Hypotensive shock	**Clear and lucid**	**'Clear and lucid' (shock is missed if we don't touch the patient)**	**Altered mental state(restless / combative)**
Capillary refill time	**Normal (<2 sec)**	**Increased (>2s)**	**Prolonged (mottled skin)**
Extremities	**Warm & pink**	**Peripheries – cold**	**Cold & clammy**
Peripheral pulse volume	**Normal**	**Weak and thread**	**Feeble / absent**
Blood pressure	**Normal**	**Normal systolic pressure but increasing diastolic pressure, narrowed pulse pressure, postural hyotension**	**Narrowed pulse pressure / hypotension / BP not recordable**
Respiratory Rate	**Normal**	**Tachypnoeic**	**Metabolic acidosis/ Kussmaul's breathing**
Heart rate	**Normal**	**Increased**	**Severe tachycardia along with bradycardia in late shock.**

CRITERIA FOR ADMISSION

Warning Signs	**Any one of the warning signs**
Signs &symptoms linked to hypotension	**Dehydrated patient, not able to swallow oral fluids , giddiness , postural hypotension, profuse perspiration, dropouts, hypotension and cold extremities.**
Bleeding	**Spontaneous bleeding irrespective of platelet count.**
Organ Impairment	**Renal/ Hepatic/ Neurologic/ Cardiac.**
Investigations	**Increasing hematocrit, pleural effusion, ascites/ asymptomatic gall bladder thickening.**
Co-existing conditions	**Pregnancy, comorbities like Diabetes , Hypertension, CAD, overweight or obesity, infancy \ geriatric age.**
Social circumstances	**single, far from health services, without reliable modes of transport.**

Management[23]

- Management of febrile phase
- Management of the DHF/DSS

Management of febrile phase

- Rest, plenty of oral fluids
- **Control of fever**: Tepid sponging, Paracetamol 15mg/kg per day in 4 divided doses every 6hrs.
- **Diet support**: Soft and bland healthy diet, plenty of fruit juices and electrolyte solutions. Drinking water alone is insufficient.
- **Supportive measures**: Domperidone in three divided doses with a total dose of one mg/ kg per day. H2 blockers in case of GI bleed. Antibiotics are unnecessary and it will even lead on to complications. Steroids are controversial and maybe harmful.
- **IV Fluids** : In doubtful cases fluids may be given IV. Response to be monitored by serial packed cell volume, blood pressure measurements & urine output. As soon as dehydration is corrected fluids must be discontinued as early as possible.

Home care

After discharge advice the patient about the warnings signs & symptoms of dengue shock syndrome, and advice them to visit nearby hospital immediately if one of the following features occur:

- Recurrence of fever
- Bleeding
- Refusal of oral feeds
- Intense thirst
- Drowsy or sleepy
- Severe vomiting
- Unbearable abdominal pain
- Altered mental state
- Cold peripheries
- Decreased urine output

Follow up

Daily till the patient is afebrile for two consecutive days.

Monitoring in follow up

History: Bleeding manifestation, urine output, pain abdomen, appetite, vomiting

Physical examination: Pulse, BP, Respiratory rate

- Lab investigations: CBC – WBC count <5000 with predominant lymphocytes and presence of atypical cells. Platelet count < one lac. Rising hematcrit. LFT – in case a patient has altered sensorium.

MANAGEMENT OF DHF/DSS

GENERAL MEASURES INCLUDES:

- ✓ In case of shock or impending shock, give oxygen through face mask or through nasal cannula.
- ✓ Frequent monitoring of vital signs
- ✓ In case of bleeding, take appropriate steps to control bleeding.
- ✓ If necessary sedatives can be used but care should be taken not to use long acting one.
- ✓ Blind invasive procedures should be avoided.
- ✓ Proper nursing care.

MONITORING PARAMETERS:

- ✓ Vitals should be assessed every half to one hour till patient becomes stable and then every one to two hours afterwards
- ✓ Amount of urine.
- ✓ Serum sodium, potassium and arterial blood gases should be taken six to twelfth hourly.

- ✓ Input and output chart.
- ✓ Haematocrit and platelet count should be checked every four to six hours till the patient becomes stable
- ✓ Weight chart
- ✓ Liver function parameters.

INVESTIGATIONS:

- ✓ Platelet count and haematocrit.
- ✓ Plasma glucose
- ✓ Blood grouping and cross matching
- ✓ Serum electrolytes
- ✓ Arterial blood gas
- ✓ Liver function parameters
- ✓ Renal function test
- ✓ Coagulation profile

FLUID MANAGEMENT:

IV fluid type: Isotonic salt solution (Ringer's lactate or normal saline)

Fluid rate: minimal amount needed to effectively maintain the circulatory volume since excess of fluids will cause fluid leakage in to pleural and peritoneal spaces.

Initial fluid rate:

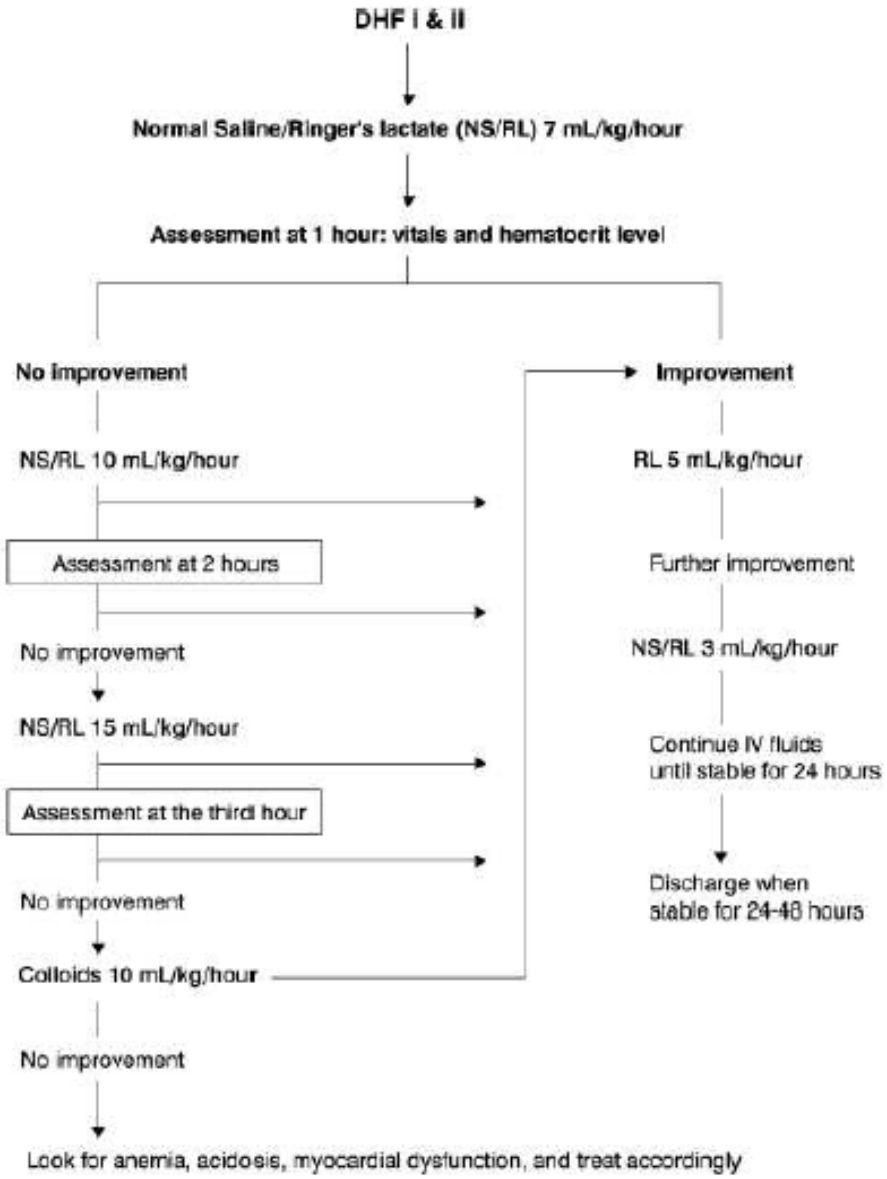
- ✓ Dengue shock syndrome grade 3- 10ml/kg/hr for one to two hours.
- ✓ Grade 4 -20ml/kg/hr or free flow iv bolus till the blood pressure becomes normal and then titrate the rate to 10ml/kg/hr for about one to two hrs.
- ✓ No shock – we should have normal maintenance of fluids.

BLOOD AND PLATELET TRANSFUSION:

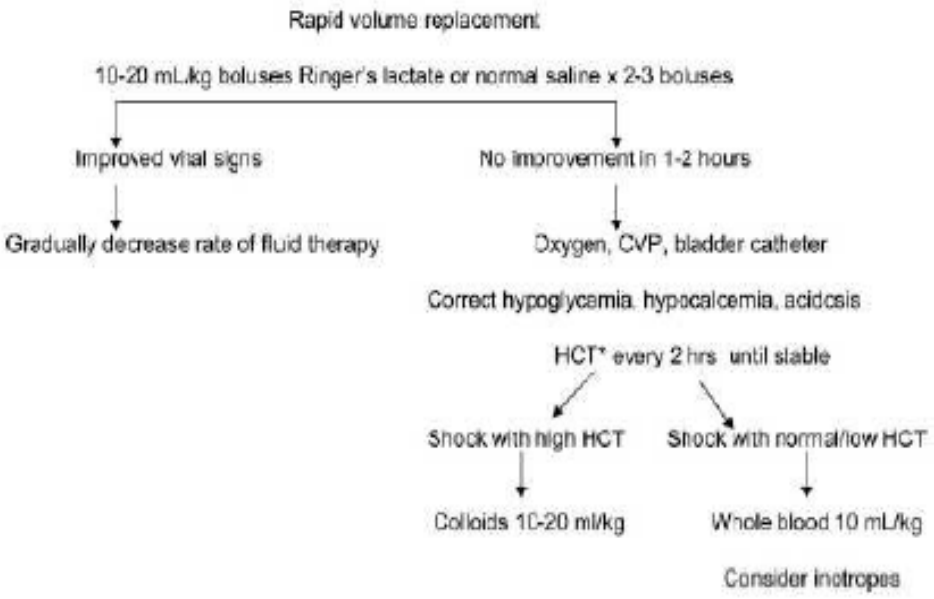
1. INDICATIONS FOR BLOOD TRANSFUSION
   - ✓ Significant blood loss > 10%
   - ✓ Hemolytic picture
   - ✓ occult internal haemorrhages
   - ✓ DOSE: fresh whole blood – 10ml/kg/dose, packed cells- 5ml/kg/dose.
2. INDICATIONS FOR TRANSFUSION OF PLATELETS
   - ✓ profound bleeding with reduced platelet count
   - ✓ Platelets <10,000/mm^3

About 0.5% of DHF cases require transfusion of platelets and that too the platelets usually return to normal within 7 to 10 days.

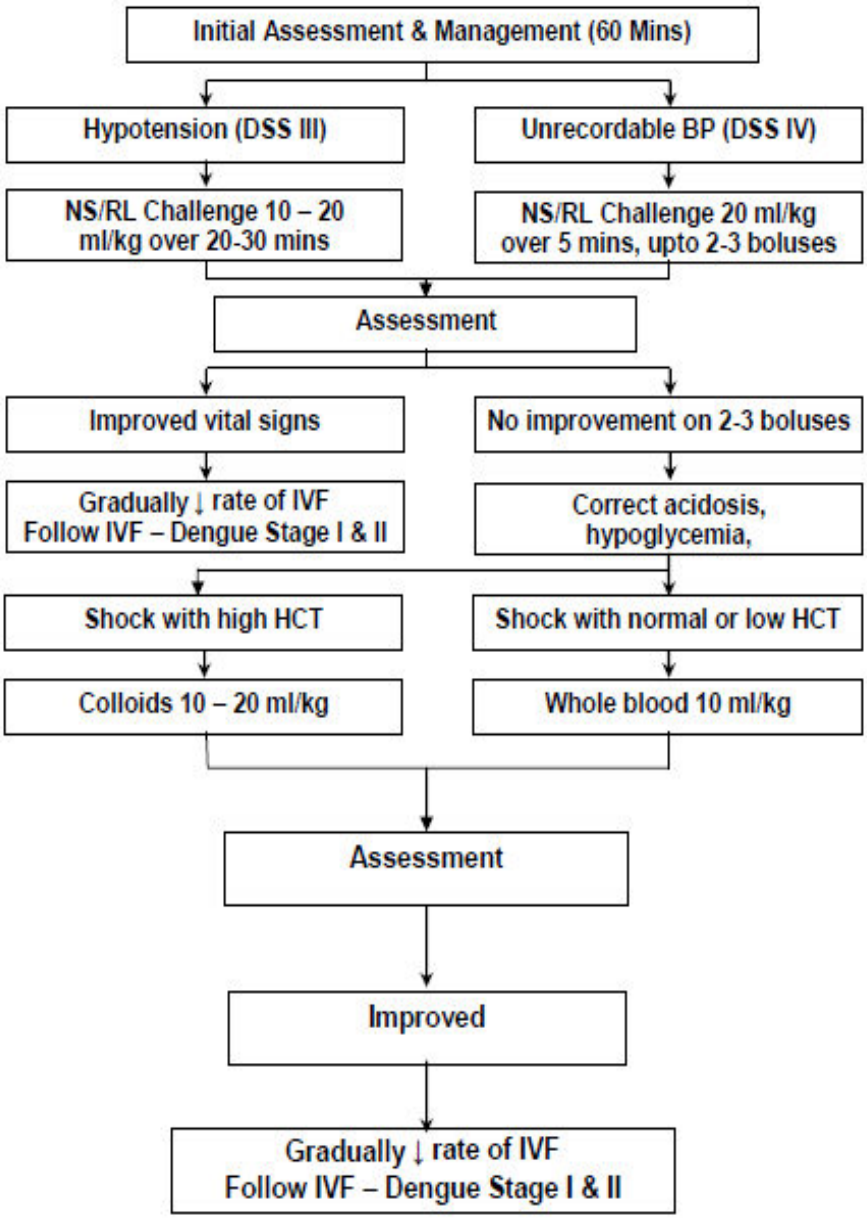
Intravenous fluid infusion algorithm in DHF[22]



Algorithm for management of dengue haemorrhagic fever[24]



Algorithm for the management of DSS[25]



Treatment of complications

1. **Electrolyte imbalance**
    a. Hypocalcemia – correction can be done with 10% Calcium gluconate 1 ml/kg per dose slow IV sixth hourly.
    b. Hyponatremia – corrections can be done with normal saline or hypertronic saline.
2. **Fluid overload** – Common causes of fluid overload should be avoided, includes:
    a. Excessive usage of hypotonic solutions.
    b. No reduction in the IV fluid rate even after initial resuscitation.
    c. Aggressive IV fluids infusion early in the febrile period.
    d. Fluid replacement for blood loss in cases of occult bleeding.
    e. Liberal fluid removal with the help of colloids or dialysis.

3. Massive pleural effusions and ascites

a. close monitoring of IV fluids
b. small doses of frusemide can be tried. Avoid using insertion of intercoastal tubes& tracheal intubation.

4. Consumption coagulopathy

Heparin and cryoprecipitate at the dosage of 1.5 units per 5 kg body weight, which is succeeded by platelets transfusion at the dosage of 4units/m^2 or 10-20ml/kg within 1 hr and fresh frozen plasma at the dosage

of 10 -20ml/kg careful clinical assessment and periodic coagulation profile, are essential.

DISCHARGE CRITERIA:

- ✓ Afebrile for atleast 24 hrs without the usuage of antipyretics
- ✓ Stable vital parameters for a minimum period of 3 days after recovered from shock
- ✓ No internal or external bleeding evidences
- ✓ Adequate urine output
- ✓ Platelets >100,000/mm^3
- ✓ Normal haematocrit values
- ✓ No evidence of ascites/respiratory distress

IV fluid should be discontinued with stable vital signs and with haematocrit levels falls to 40% approximately. Adequate urine flow suggests effective circulation. Extravasated fluids will reabsorb 48 hrs after recovering from shock and therefore if more fluid is given during this time, hypervolemia, pulmonary oedema and heart failure will occur. Importantly a reduction in packed cell volumes occurring in the last stage should never be assumed due to occult haemorrhage. The resumption of the appetite is considered as a very good recovery sign in diseased individual.

Prevention & Control

Nowadays, no particular drug and vaccine against dengue virus is present. Control is largely dependent up on the control of vector.

I. Personal protection: Protective clothes, repellents, insecticide coated mosquito nets/curtains.
II. Environmental factors: good supply of drinking water, roofing of above head tanks and also the underground drainage system.
III. Biological control: with the help of "Gambria affinis and Peorilia reticulate", larvivorous fish.
IV. Chemical control: using '1% temephos granules and space sprayers like malathion, pirimiphos'. Insect growth regulators can also be tried.

Vaccines

Dengue vaccine trial using an quadrivalent live attenuated vaccine was conducted in Thailand. In that trial, after completing the 3rd dose 90% of individuals were seroconverted. It sympathesises that the vaccine has got moderate and at the same time improved reaction capacity with higher seroconversion rates against 4 serotypes of dengue. After the two doses of vaccine was administered in young children, it produces about 80 to 91% of seroconversion rate to all the four dengue subjects. The vaccine introduced by the 'Walter Reed Army Institute of Research in America' also got similar

seroconversion in adults. The molecular mechanism of attenuation by the two vaccines is not clearly known. It is therefore assumed that interference with replication and also interference with immune stimulation is responsible for the imbalanced immune responses and thereby causing incomplete protection and enhanced disease severity.

Prognosis[3,4,5]

If initial recognition & monitoring was not done properly, there was a significant morbidity and mortality. The mortality of DHF/DSS was about 45 to 55% if left untreated. Early disease recognition, close monitoring and adequate fluid management alone have reduced the mortality to about 2%. When shock is noticed with the help of pulse pressure starting to drop down and immediately IV fluids are infused, the outcome is usually very good. Recovery was also rapid and almost all of the patients recovered within one to two days without having much complications. The outcome is poor when the patient developed cold peripheries. Many of the mortality from DHF/DSS are due to excessive bleeding, refractory shock, excessive fluid management and fulminent hepatic failure.

Unusual manifestations

- Hepatitis
- Glomerulonephritis
- Encephalitis
- Myocardial dysfunction

Dengue Fever - Differential Diagnosis

Conditions that mimic the febrile phase of dengue infection	
Flu-like syndromes	Influenza, measles, Chikungunya, infectious mononucleosis , HIV seroconversion illness
Illnesses with a rash	Rubella, measles, scarlet fever, meningococcal infection, Chikungunya, drug reactions
Diarrhoeal diseases	Rotavirus, other enteric infections
Illnesses with neurological manifestations	Meningo/encephalitis febrile seizures

Dengue Fever - Differential Diagnosis (Contd..)

Conditions that mimic the critical phase of dengue infection	
Infectious	Acute gastroenteritis, malaria, leptospirosis, typhoid, viral hepatitis, acute HIV seroconversion illness, bacterial sepsis, septic shock
Malignancies	Acute leukemia and other malignancies
Other clinical pictures	Acute abdomen – acute appendicitis, cholecystitis, perforated viscus Diabetic ketoacidosis Lactic acidosis Leukopenia and thrombocytopaenia ± bleeding Platelet disorders Renal failure Respiratory distress (Kussmaul's breathing) Systemic Lupus Erythematosus

LIVER INVOLVEMENT IN DENGUE FEVER

Atypical forms of dengue infection are numerous. Notable one is liver dysfunction. Liver injury is due to either direct injury to hepataocytes by virus itself or indirectly due to an immune mediated damage to hepatocytes. Even though liver is usually not affected by virus, numerous pathological changes like "steatosis, centrilobular cell necrosis & monocyte implantation in the portal tract" is noticed.

Chen HC et al[51] in 2004 reported that there was a "significant correlation between T lymphocyte activation and liver dysfunction in immunocompetent mice". In one study, about three tenths of all patients are presented with liver dysfunction. Liver dysfunction is considerably higher in Asian populations ranging from 30 – 90%. The rate of liver dysfunction in patients with shock is higher than the patient without shock.

Recently Pancharoen et al[34] reported that 'average of SGOT and SGPT enzyme levels were significantly raised in patients of severe dengue infections'.

Hepatic involvement is not that much uncommon in dengue fever as seen in literature since 1975. Most common abnormality in liver function test is increased transaminases and they are involved in metabolism of amino acids. AST is found to be higher than that of ALT levels. In more

than 90% of patients with dengue fever, the virus itself initiates some inflammatory responses which causes hepatic parenchymal damage and release of transaminases in to systemic circulation.

Table I : Primary outcomes according to hepatitis severity within 2 categories of diagnosis

Diagnosis Categories	Severity of hepatitis	Deaths n	Death rate (Deaths/10 day)	H.R (95% CI; UCI, LCI)^	P value (Difference in death rate)!	LOS ± SD	P value
Dengue fever (n = 517)	Mild to Moderate Hepatitis (n = 436)	3	0.019	2.97(0.48,18.6)	0.283	3.50 ± 1.54	<0.025
	Severe hepatitis (n = 81)	3	0.093			3.96 ± 2.27	
DHF/DSS (n = 82)	Mild to Moderate Hepatitis (n = 60)	3	0.010	5(1.3,16)	0.003	4.60 ± 2.87	.212
	Severe hepatitis (n = 22)	9	0.073			5.60 ± 3.85	

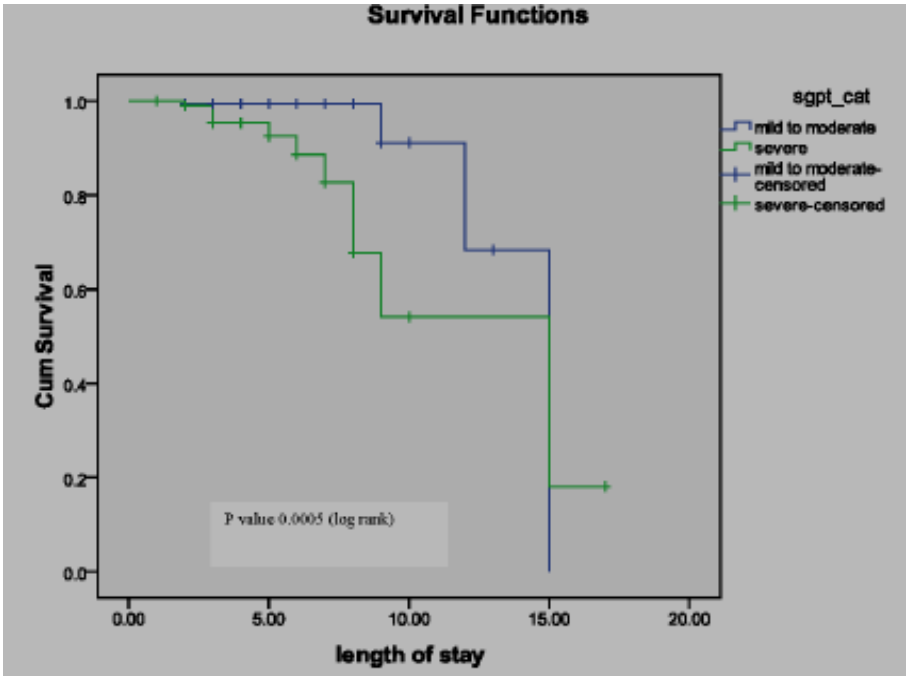
^H.R = Hazard Ratio, UCI = Upper confidence interval, LCI = Lower confidence interval
! Log Rank value

Table II : Complications in 2 hepatitis groups

Complications	Mild to moderate (n = 496)	Severe hepatitis (n = 103)	P value
Bleeding[1] (n)	3	7	<0.001[6]
Renal failure[2] (n)	8	8	0.002
Encephalopathy[3] (n)	7	11	0.02
Shock[4] (n)	6	2	0.40[6]
Acalculus cholecystitis[5] (n)	14	7	0.04

1. Either mucosal bleeding (epistaxis or gum bleed) or Gastrointestinal (GI) bleed
2. Acute Renal Failure (ARF) was defined as rise of creatinie >3 times(13)
3. Encephalopathy was defined as altered mental status for > 8 hours (drowsiness, lethargy, agitation, or coma)(19)
4. Shock was defined as Hypotension (defined as systolic pressure < 90 mm Hg)(14)
5. Acalculus cholecystitis was defined as inflammation of gall bladder without stone on US (15)
6. Anayzed by fischer exact test

Figure I : Kaplan-Meir curve for survival over the period of time in 2 groups of hepatitis patients



Numbers at risk in each group at 5 day interval

	Days			
Hepatitis	0	5	10	15
Mild to Moderate (n)	305.5	60	4	1
Severe (n)	70	21	3.5	2.50

'Prakasah et al[52] postulated that the fatal hepatitis will cause an important cofactor for case fatality in dengue patients'. They also found that patients with severe hepatitis are likely to be more prone for renal failure, encephalopathy, severe bleeding and acalculous cholecystitis.

Kho CH et al[30] came with the report that those patients with higher levels of AST/ALT levels are likely to have severe bleeding tendencies.

Nguyen et al[31] found that those patients with gastrointestinal hemorrhage are having elevated AST and ALT levels. They also found that in addition to thrombocytopenia, deranged hepatic function may have a role in bleeding.

Acalculous cholecystitis and encephalopathy are significantly higher in individuals with fatal hepatitis.

"Prakash et al[52] found that that when liver function tests are damaged, dengue fever should be ruled out apart from routine hepatotrophic virus".

Arun Sedhain et al[45] study also confirmed that levels of AST and ALT were significantly higher in Dengue Hemorrhagic Fever (DHF) patients than Dengue Fever (DF) and that too AST levels were greater than ALT levels, as opposed to viral hepatitis.

Table : 3 Laboratory parameters of DF and DHF patients.

Variables	DF (n=329)		DHF (n=85)		*P* value
	Count	Percentage	Count	Percentage	
Platelet <50 000	32	9.73%	43	51.19%	<.0001
ALT more than 50	258	78.42%	81	96.43%	<.0001
AST more than 50	177	53.80%	62	73.81%	<.0001

They also found out that liver involvement is more severe in cases of DEN-3 and DEN-4 viruses. Many studies used an immunohisto chemical method to detect the presence of dengue antigens in liver specimens. They predominantly used antibodies directing against dengue E protein and recently antibody against dengue NS3 protein is also used. Majority of the studies detected the presence of dengue antigen in hepatocytes.

Table : 4 Ultrasonologic manifestations of DF and DHF patients.

Variables	DF (n=329)		DHF (n=85)		*P* value
	Count	Percentage	Count	Percentage	
Hepatomegaly	100	30.40%	62	72.94%	<.0001
Thickened gall bladder	20	6.08%	22	25.88%	<.0001
Third space loss	18	5.47%	84	98.82%	<.0001

Table 5 : Comparison of certain characteristics in dengue hemorrhagic fever and dengue fever

S. No.		DHF(n=22)	DF(n=48)	p Value
1	Av. Platelet (per mm3)	29,000±23000	38,000±25000	0.187
2	Av. Serum Bilirubin (in mg%)	0.88±0.38	1.01±0.79	0.517
3	Av. SGPT (in units/L)	138±206	132±219	0.911
4	Av.SGOT (in units/L)	239±295	283±541	0.734
5	Av. Alk. Phosphatase (in units/L)	76.6±33	94±93	0.412
6	Hepatosplenomegaly	4/22(20%)	15/48(31%)	------
7	Leucopenia	2/22(10%)	4/48(8.3%)	-------

Values showing mean±std deviation or n(%)

Table 6 : Clinical characteristics and lab parameters in the study subjects

S. No.	Parameter	Value
1	Av. Platelet Count (per mm^3)	35,000±25000
2	Av. Serum Bilirubin(mg%)	0.9±0.6
3	Av. SGPT(units/L)	133 ±214
4	Av. SGOT(units/L)	267 ±460
5	Av. Alkaline Phosphatase(units/L)	89 ±80
6	SGPT > 2xULN	34(48%)
7	SGOT > 2x ULN	64(91%)
8	Ascitis	42(60%)
9	Hepatomegaly	36(50%)
10	Splenomegaly	15(21%)
11	Pleural effusion	10(15%)
12	Leucopenia	7(10%)

Values showing mean±std deviation or n(%)

Presence of vomiting from day one may indicate the possibility of hepatic dysfunction.

PT and aPTT derangements are mild with aPH being more affected than PT.

AST and ALT values were significantly elevated in individuals with any of the following features:

1. Patients with dengue hemorrhagic fever or secondary dengue.
2. Thrombocytopaenia or an increased haematocrit.
3. Nausea / Vomiting
4. Hepatomegaly
5. Bleeding tendencies

"Kho et al reported that SGOT begins to raise from 3rd day of illness reaches a peak on 8th to 9th day of illness & normalizes at around third week".

PATHOGENESIS OF HEPATIC DYSFUCTION[29,41]

Histological changes in liver because of dengue include:

1. Hepatocellular necrosis
2. Councilman bodies
3. Kupffer cell hyperplasia and destruction
4. Micro vesicular steatosis
5. Cellular infiltrates at the portal tract

In dengue, hepatocellular necrosis most commonly involves the mid zonal area and at times centrilobular area. This is because mid zonal area hepatocytes are more prone to anoxic injury or immunological injury or sometimes the virus may preferentially attack cells in this zone.

Dengue viral RNA can be detected in mid zonal hepatocytes using an PCR method of archives paraffin embedded autopsy tissues. Pathological changes seen in liver in dengue liver is similar to that of yellow fever[26,27,28]. But hepatocellular necrosis is more severe and extensive in yellow fever. Dengue viral antigens are seen mainly as focal cytoplasmic foci and large perinuclear inclusions whereas yellow fever antigenic particles were uniformly distributed throughout the cytoplasm.

Dengue infection of 'HePG2 cells' causes expression of only a small amount of infections particles and it causes a slight rise in the amount of antigen enclosing cells over the period of time. But as against the dengue fever, yellow fever viruses multiplied in high amount of titres and it infects almost every susceptible cells in the liver.

'Dengue virus affected cells rapidly died as a result of apoptosis whereas yellow fever virus infected cells die lately'. Dengue fever virus can replicate both in kupffer cells and in hepatocytes though dengue virus enters the kupffer cells. Replication of virus particles in the kupffer cells are not effective. This is because viral antigenic particles enter the kupffer cells by the method of phagocytosis which usually causes viral degradation.

In order to mention the occurrence of severe disease, 'immune enhancement and virus virulence hypothesis' have been developed. Those individuals who are exposing to secondary dengue infection with another dengue virus serotype are more likely to have increased DFS/DHF. This observation can be explained by the antibody dependent enhancement therapy.

Already existing non neutralizing antibodies will form complexes within the virus particles and it will increase its uptake & replication in macrophage system of our body during secondary dengue virus infections.

During dengue infection, 'B cells, mast cells, monocytes and T.cells' produces larger amounts of cytokines. During first three days of illness, 'TNF-α, IL-2,IL-6, IFN-α' are highest in the serum whereas' IL-10, IL-5, IL-4' appears later. IFN-α protects against severe dengue infections whereas IL-6, IL-5 increases the occurrence of DHF/DSS.

"Gagnon et al (1999) have reported that CD4+ cytotoxic T cells are responsible for liver destruction in dengue fever involving a mechanism which involves bystander lyses". 'CD4+ mediated cytotoxicity' occurs via two pathways.

1. Activated CD4+ cytotoxic T cells releases perborin and granymes.
2. 'Fas on the target cell ineracts with Fas ligand on the T cells'.

MATERIAL AND METHODS

STUDY CENTRE

Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

DURATION OF THE STUDY

6 months

STUDY DESIGN

Cross sectional study

SAMPLE SIZE

60 patients

DATA COLLECTION AND METHODS

Patients have their history taken according to a questionnaire and subjected to clinical examination and patients were subjected to the investigations of complete blood count, ,plasma glucose, blood urea, serum creatinine, QBC for MP/MF, MSAT for leptospirosis, blood culture, widal, anti-HAV, HBsAg, anti HCV, Chest X-ray, USG abdomen and liver function tets.

PRODUCT / PROCEDURE / INVESTIGATION DETAILS

Serum aminotransferase levels

INCLUSION CRITERIA

Patients aged ≥18 years and dengue IgM positive.

EXCLUSION CRITERIA

Chronic liver disease, viral hepatitis (Hepatitis A,B and C), Malaria, Leptospirosis, Typhoid and history of alcohol abuse.

STATISTICAL METHODS

The statistical analysis is done based on paired chi-square and p-value is calculated using paired t-statistic.

SPONSORSHIP

No

CONFLICT OF INTEREST

None

OBSERVATIONS AND RESULTS

TABLE 1 : SEX DISTRIBUTION OF AST CATEGORY

	AST category		Total
	High	Normal	
Male	22	10	32
Female	14	14	28
Total	36	24	60

Out of 60 patients studied, males were 32 and females were 28. Chi square test was applied to test the significance between the AST levels and sex distribution. There was no significant difference ($p = 0.139$) found between the variations in the AST levels and sex distribution. This implies that AST levels does not depends upon the sex distribution.

SEX DISTRIBUTION OF AST CATEGORY

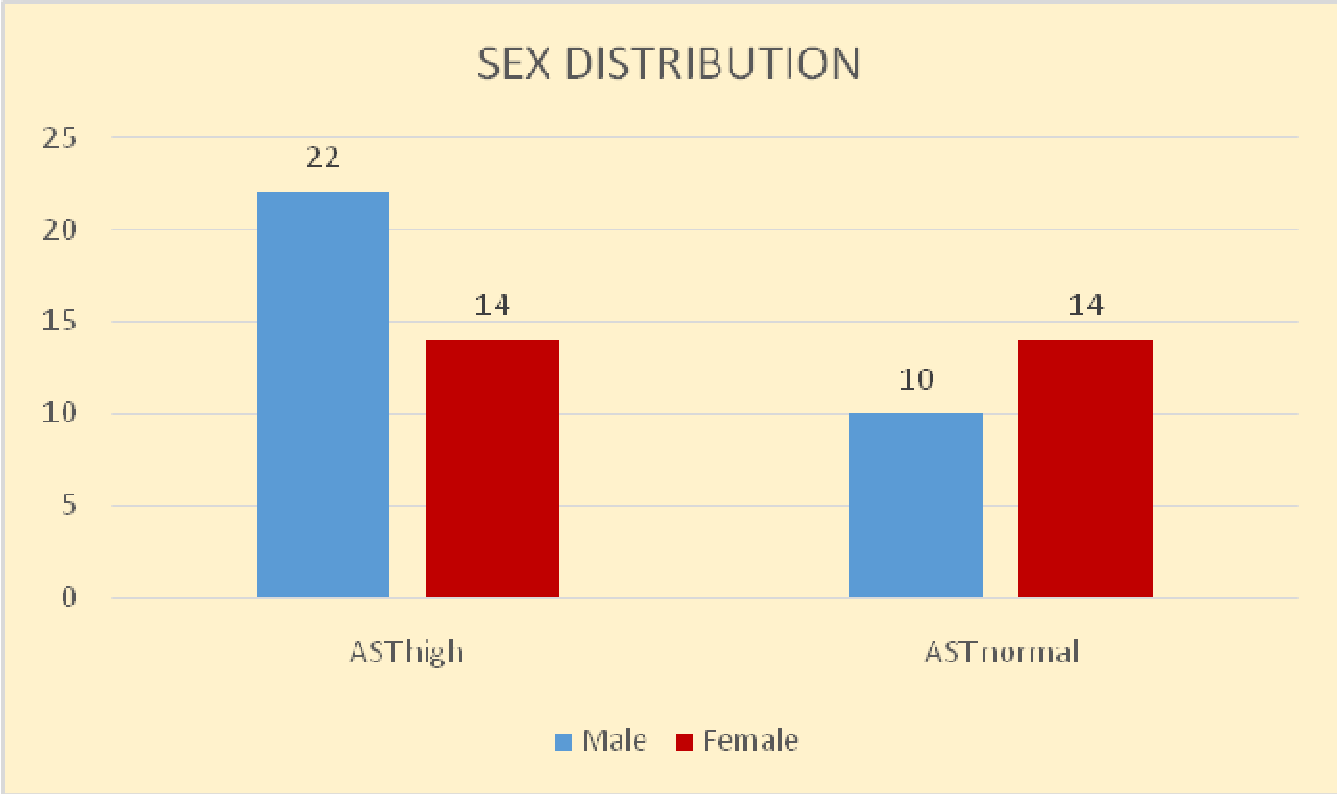


TABLE 2 : AGE DISTRIBUTION OF PATIENTS

Age Range	No.of Patients	Percentage
18 – 25	12	20%
26 – 30	8	13%
31 – 35	5	8%
36 – 40	17	28%
41 – 45	7	12%
46 – 50	7	12
51 – 55	4	7%

Out of 60 patients studied, most of them were in the age group of 36 – 40 years (n=17) and the least number in the age group of 51 – 55 years (n=4).

AGE DISTRIBUTION OF PATIENTS

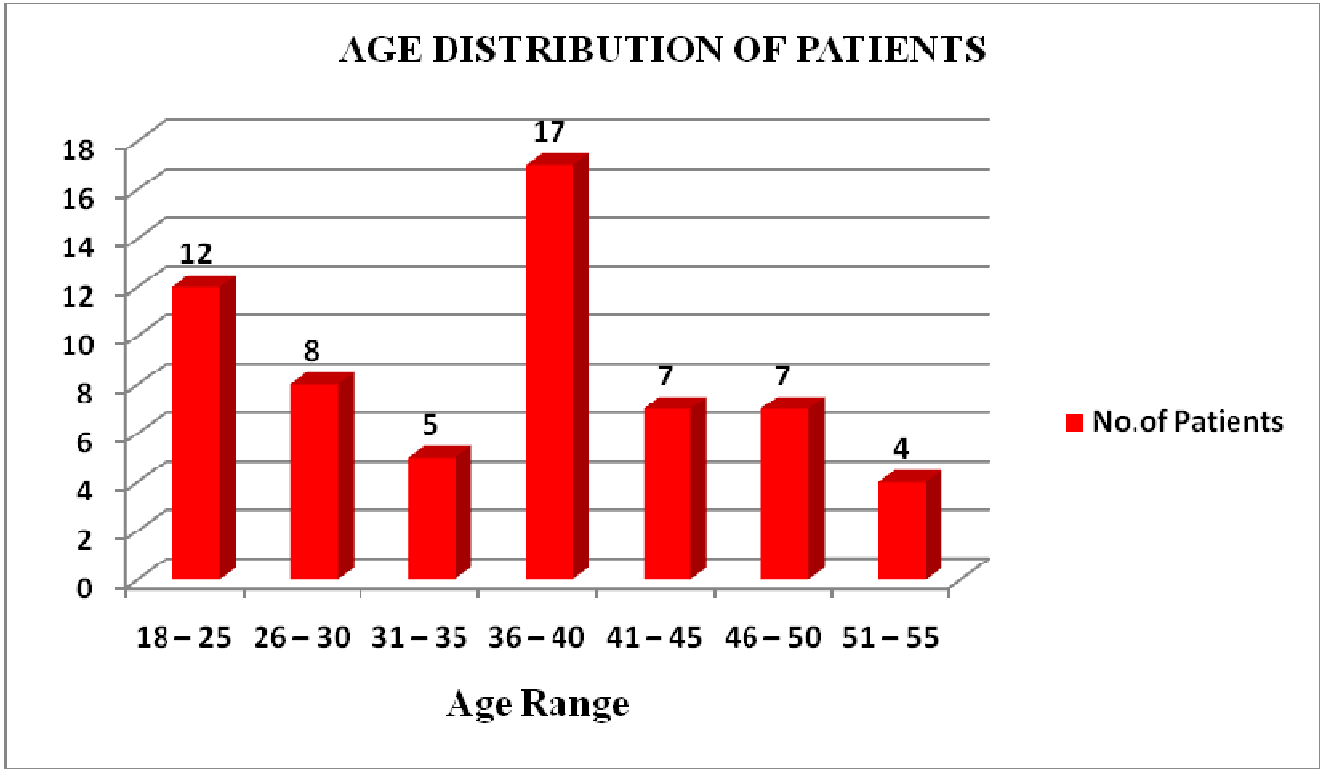


TABLE 3 : SEX DISTRIBUTION OF PATIENTS

Age Range	Male	Female	Total
18 – 25	5	7	12
26 – 30	4	4	08
31 – 35	4	1	05
36 – 40	9	8	17
41 – 45	3	4	07
46 – 50	6	1	07
51 – 55	1	3	04
Total	32	28	60

Out of 60 patients studied, highest number (n=17) is in the age group of 36 – 40 of which 9 patients were male and 8 patients were female.

SEX DISTRIBUTION OF PATIENTS

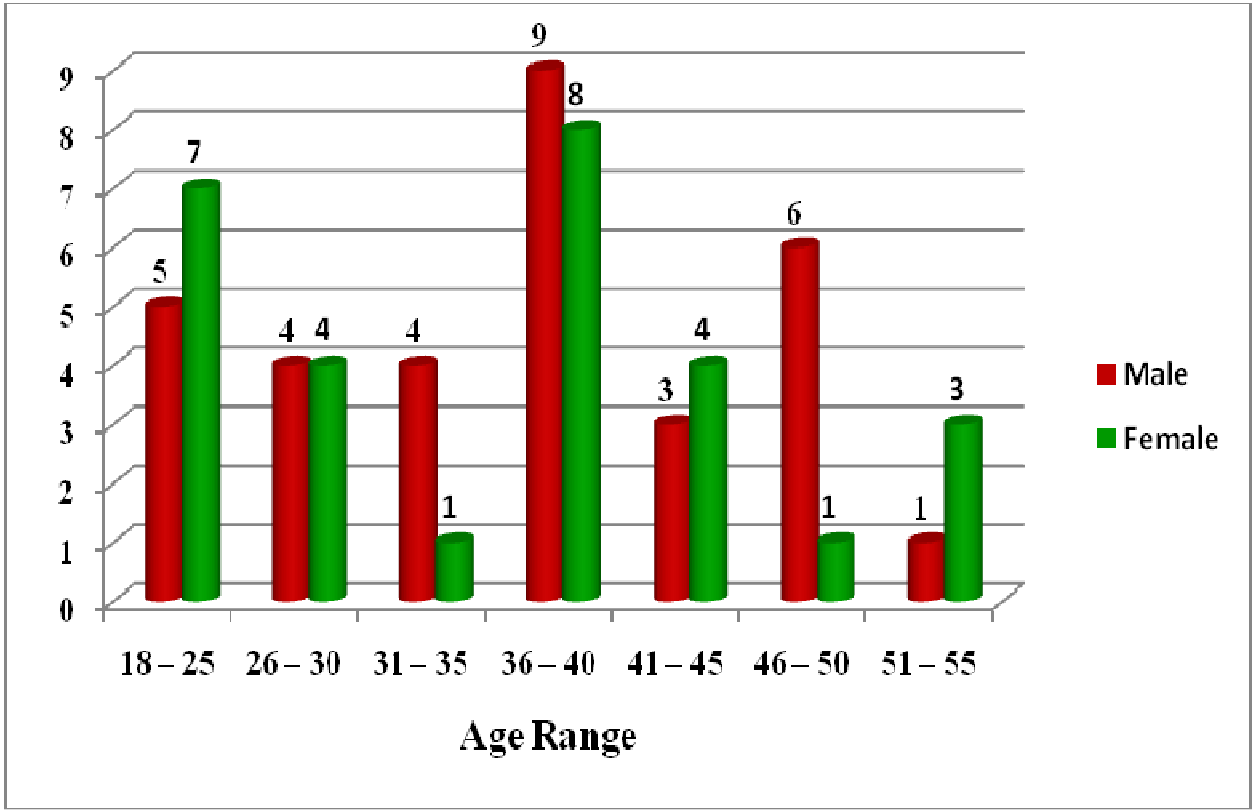


TABLE 4 : SIGNIFICANCE BETWEEN AST LEVELS AND BLEEDING TENDENCIES

		Bleeding		Total
		Present	Absent	
AST category	High	29	7	36
	Normal	0	24	24
Total		29	31	60

Chi square test was applied to test the significance between the AST levels and bleeding tendencies. There was a significant difference ($p = 0.000$) found between the variations in the AST levels and the bleeding tendencies. This implies that bleeding tendency depends upon the levels of AST.

SIGNIFICANCE BETWEEN AST LEVELS AND BLEEDING TENDENCIES

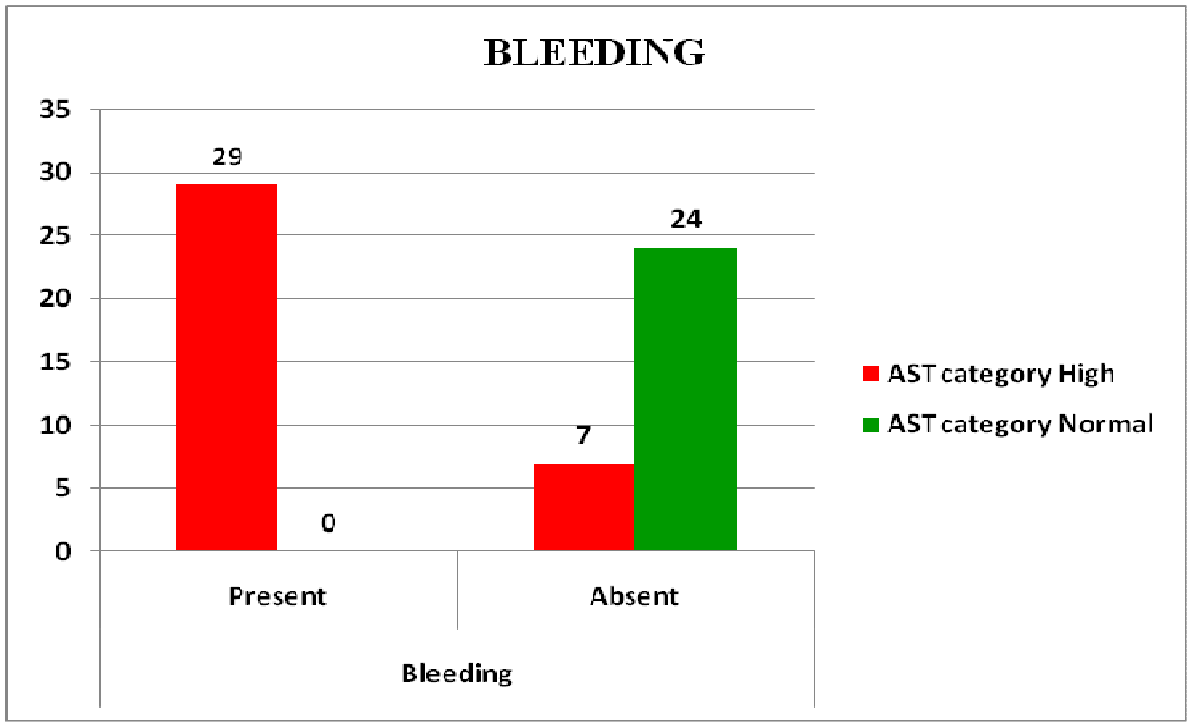


TABLE 5 : SIGNIFICANCE BETWEEN AST LEVELS AND SHOCK

		Shock		Total
		Present	Absent	
AST category	High	13	23	36
	Normal	0	24	24
Total		13	47	60

Chi square test was applied to test the significance between the AST levels and shock. There was a significant difference ($p = 0.001$) found between the variations in the AST levels and shock. This implies that shock depends upon the levels of AST.

SIGNIFICANCE BETWEEN AST LEVELS AND SHOCK

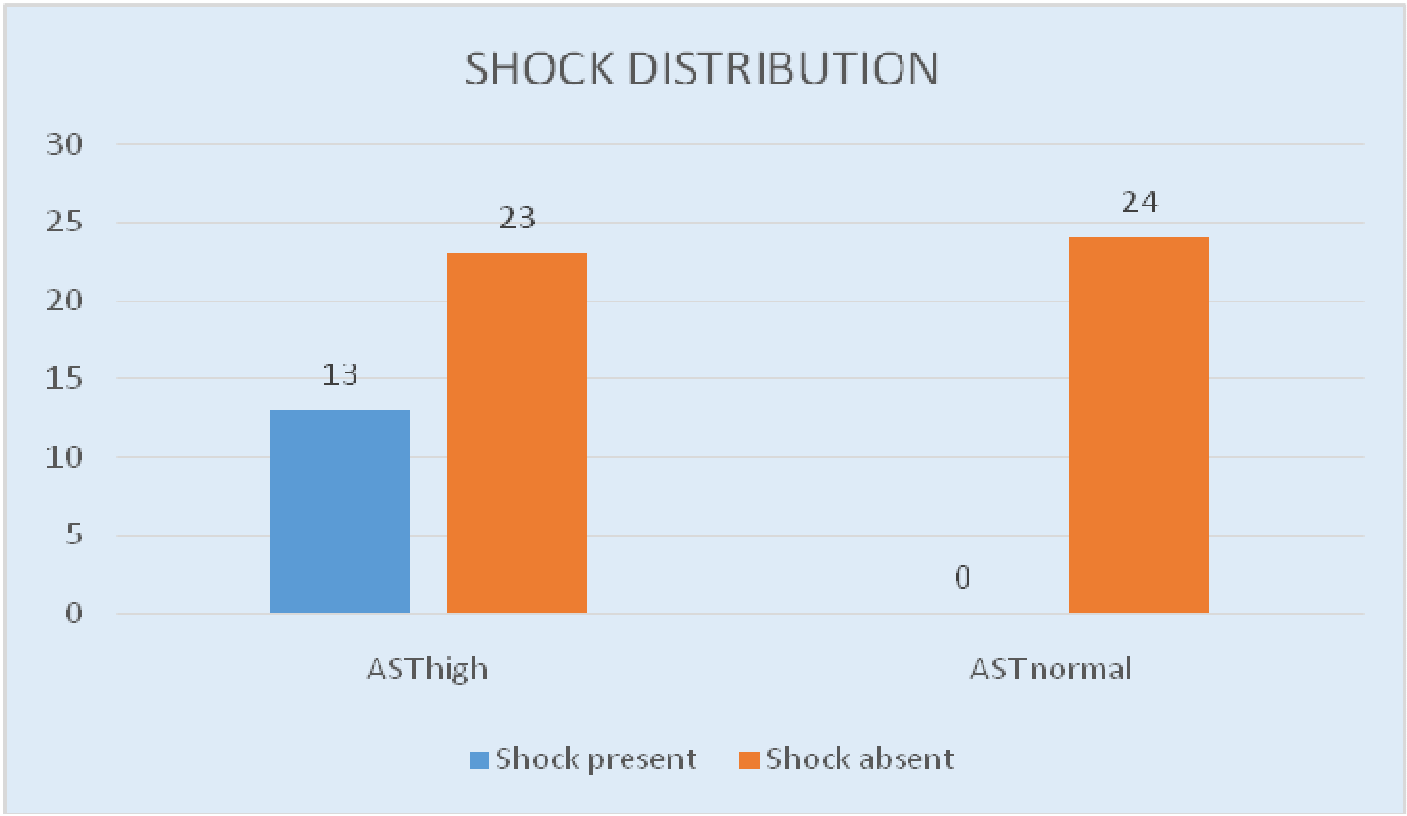


TABLE 6 : SIGNIFICANCE BETWEEN AST LEVELS AND HEPATOSPLENOMEGALY

		Hepatosplenomegaly		Total
		Present	Absent	
AST category	High	6	30	36
	Normal	0	24	24
Total		6	54	60

Chi square test was applied to test the significance between the AST levels and Hepatosplenomegaly. There was a significant difference ($p = 0.035$) found between the variations in the AST levels and Hepatosplenomegaly. This implies that hepatosplenomegaly depends upon the levels of AST.

SIGNIFICANCE BETWEEN AST LEVELS AND HEPATOSPLENOMEGALY

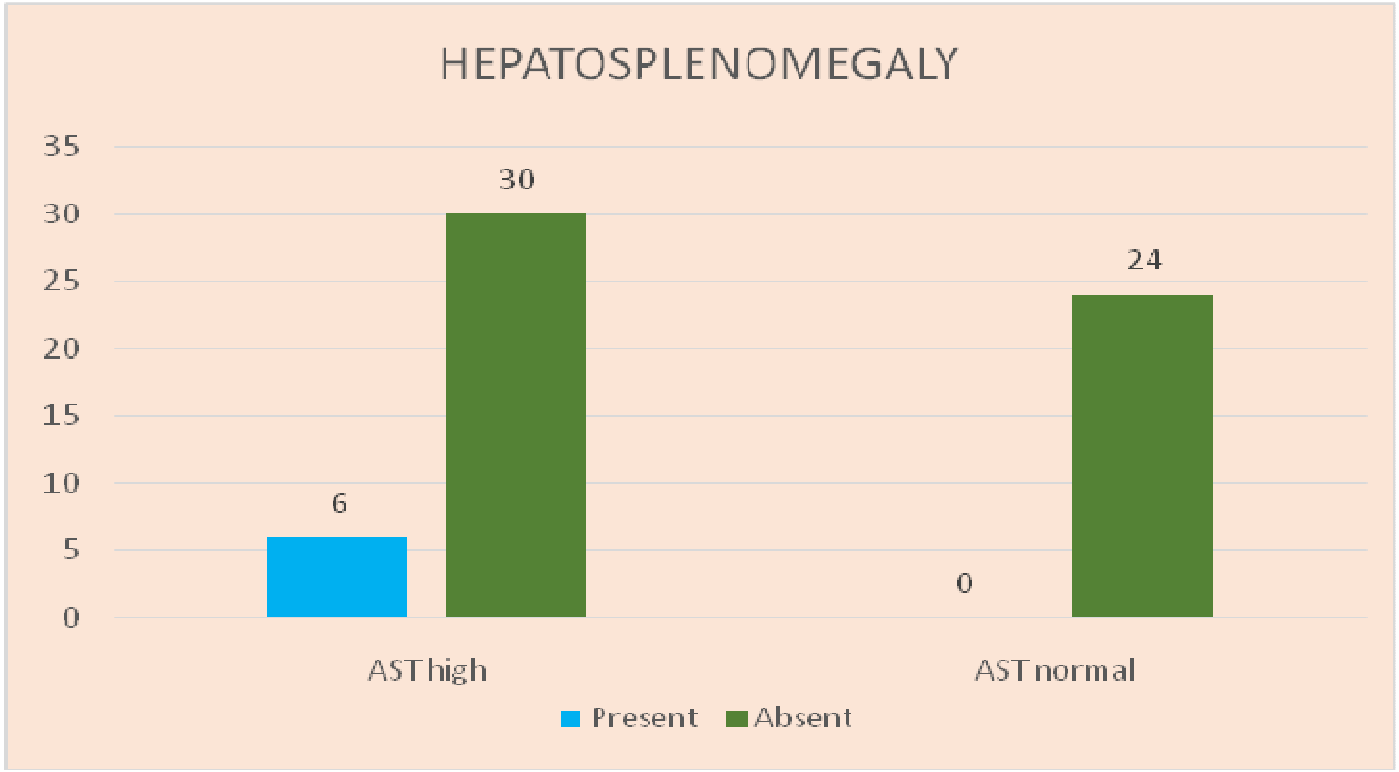


TABLE 7 : SIGNIFICANCE BETWEEN AST LEVELS AND ARDS

		ARDS		Total
		Positive	Negative	
AST category	High	6	30	36
	Normal	0	24	24
Total		6	54	60

Chi square test was applied to test the significance between the AST levels and ARDS. There was a significant difference ($p = 0.035$) found between the variations in the AST levels and ARDS. This implies that ARDS depends upon the levels of AST.

SIGNIFICANCE BETWEEN AST LEVELS AND ARDS

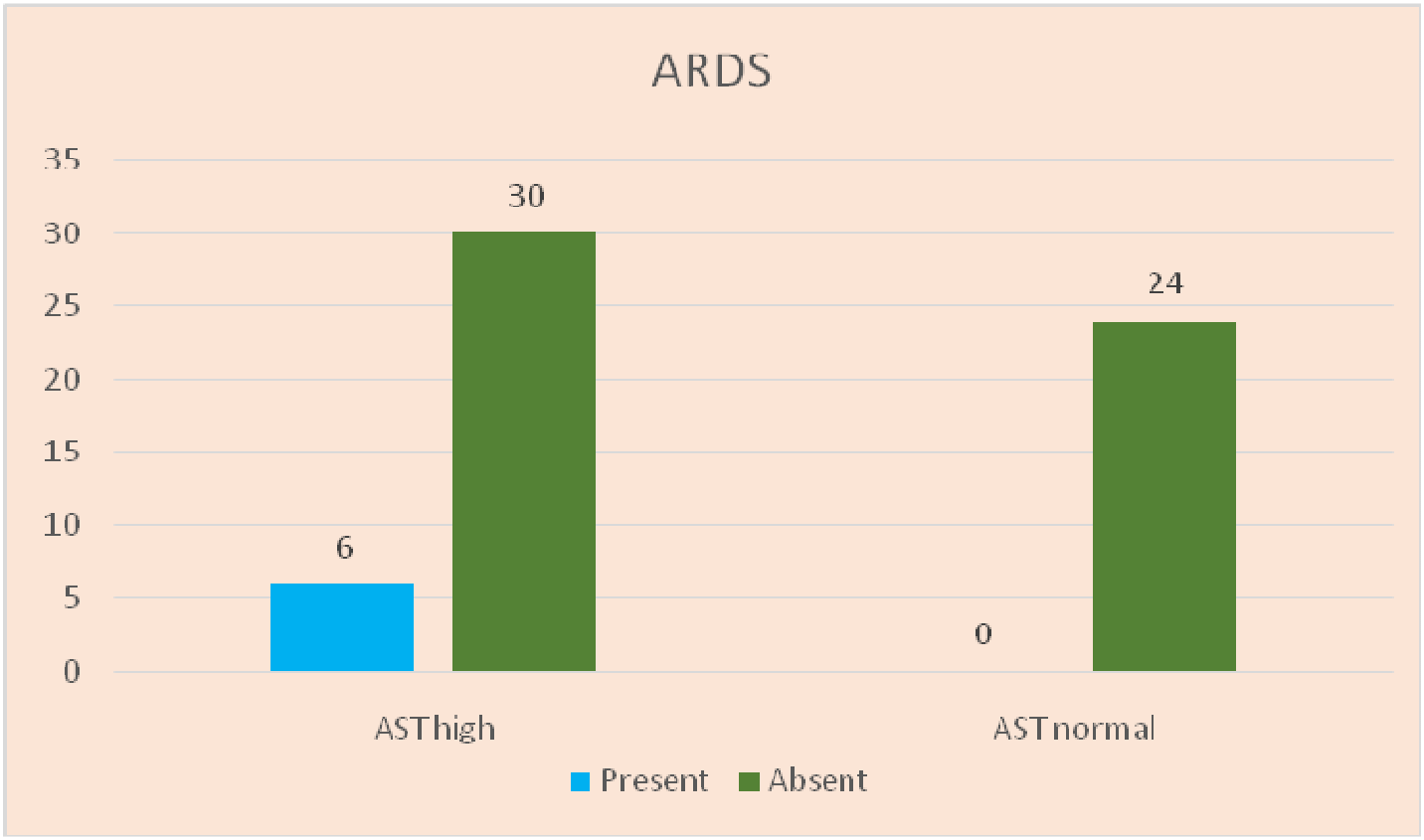


TABLE 8 : SIGNIFICANCE BETWEEN AST LEVELS AND FREE FLUID IN ABDOMEN

		Free Fluid		Total
		Present	Absent	
AST category	High	19	17	36
	Normal	0	24	24
Total		19	41	60

Chi square test was applied to test the significance between the AST levels and free fluid in abdomen. There was a significant difference ($p = 0.000$) found between the variations in the AST levels and free fluid in abdomen. This implies that free fluid in abdomen depends upon the levels of AST.

SIGNIFICANCE BETWEEN AST LEVELS AND FREE FLUID IN ABDOMEN

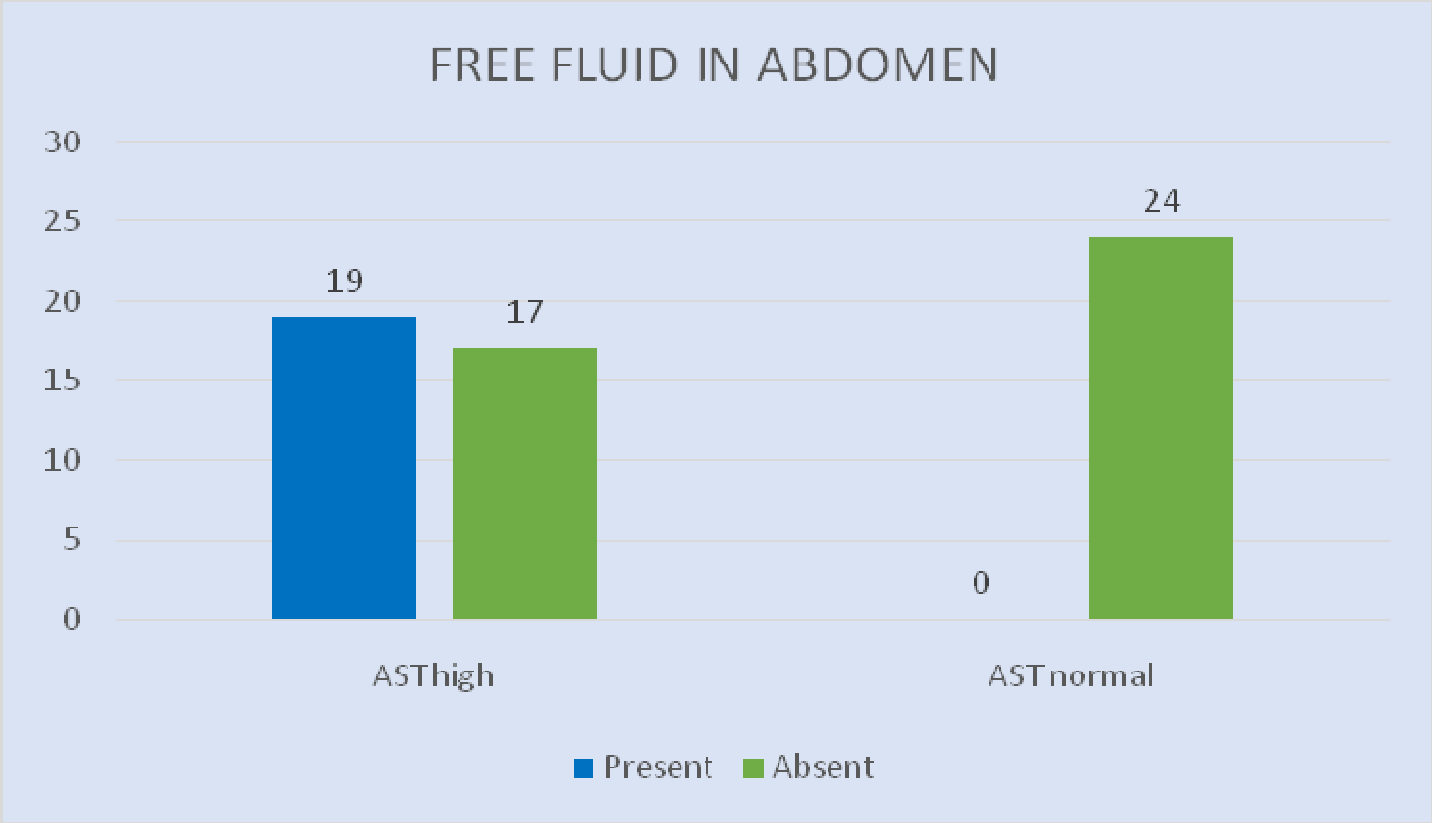


TABLE 9 : SIGNIFICANCE BETWEEN AST LEVELS AND ALCOHOLIC CONSUMPTION

		Alcoholic		Total
		Yes	No	
AST category	High	14	20	34
	Normal	4	18	22
Total		18	38	56

Chi square test was applied to test the significance between the AST levels and alcoholic consumption. There was no significant difference ($p = 0.072$) found between the variations in the AST levels and alcoholic consumption. This implies that alcoholic consumption does not depends upon the levels of AST.

SIGNIFICANCE BETWEEN AST LEVELS AND ALCOHOLIC CONSUMPTION

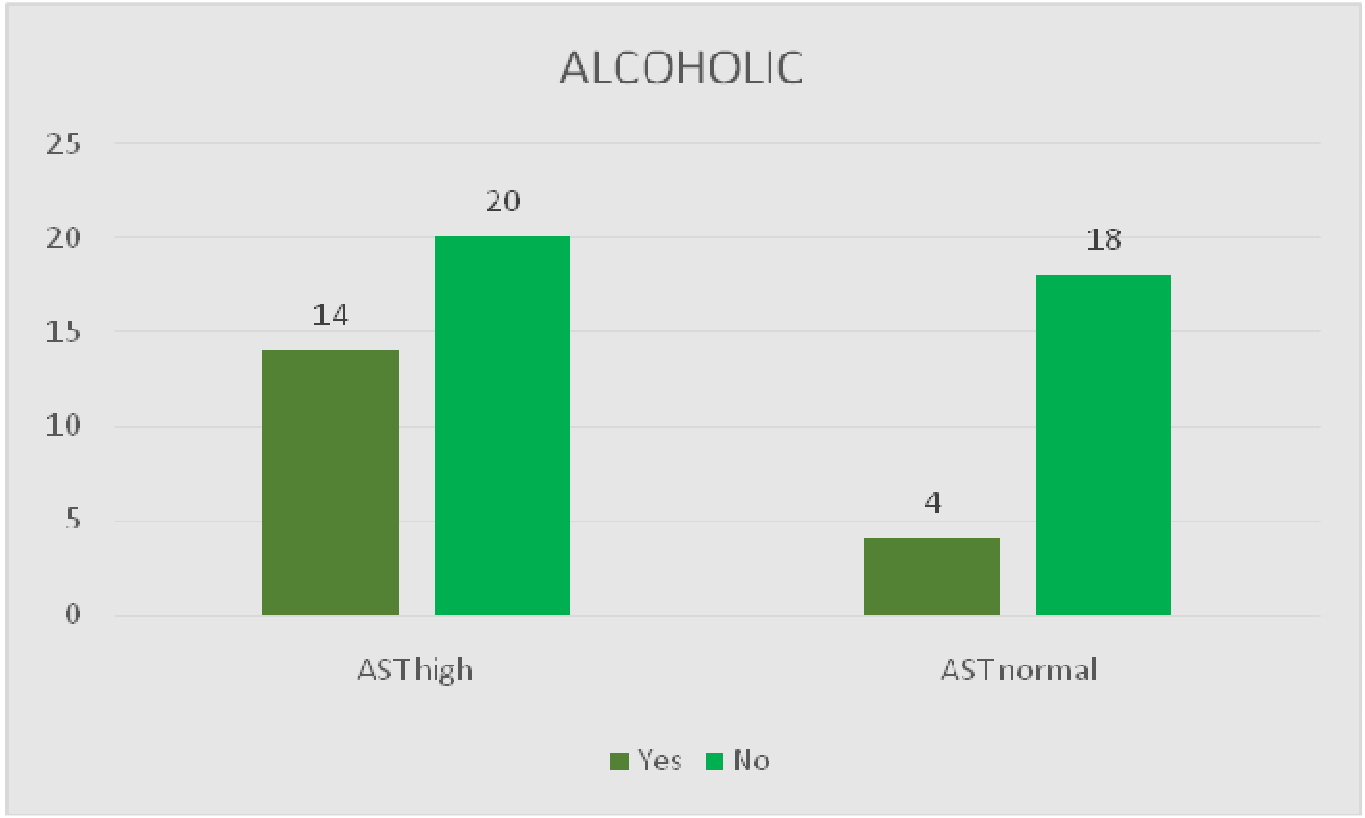


TABLE 10 : CORRELATION BETWEEN AST LEVELS AND PLATELETS

		Platelets /mm3	AST
Platelets /mm3	Pearson Correlation	1	-.306*
	Sig. (2-tailed)		.017
	N	60	60
AST	Pearson Correlation	-.306*	1
	Sig. (2-tailed)	.017	
	N	60	60
*. Correlation is significant at the 0.05 level (2-tailed).			

There was a significant negative correlation between AST levels and platelet count (r = -0.306). This implies that increase in AST levels is associated with decrease in platelets.

CORRELATION BETWEEN AST LEVELS AND PLATELETS

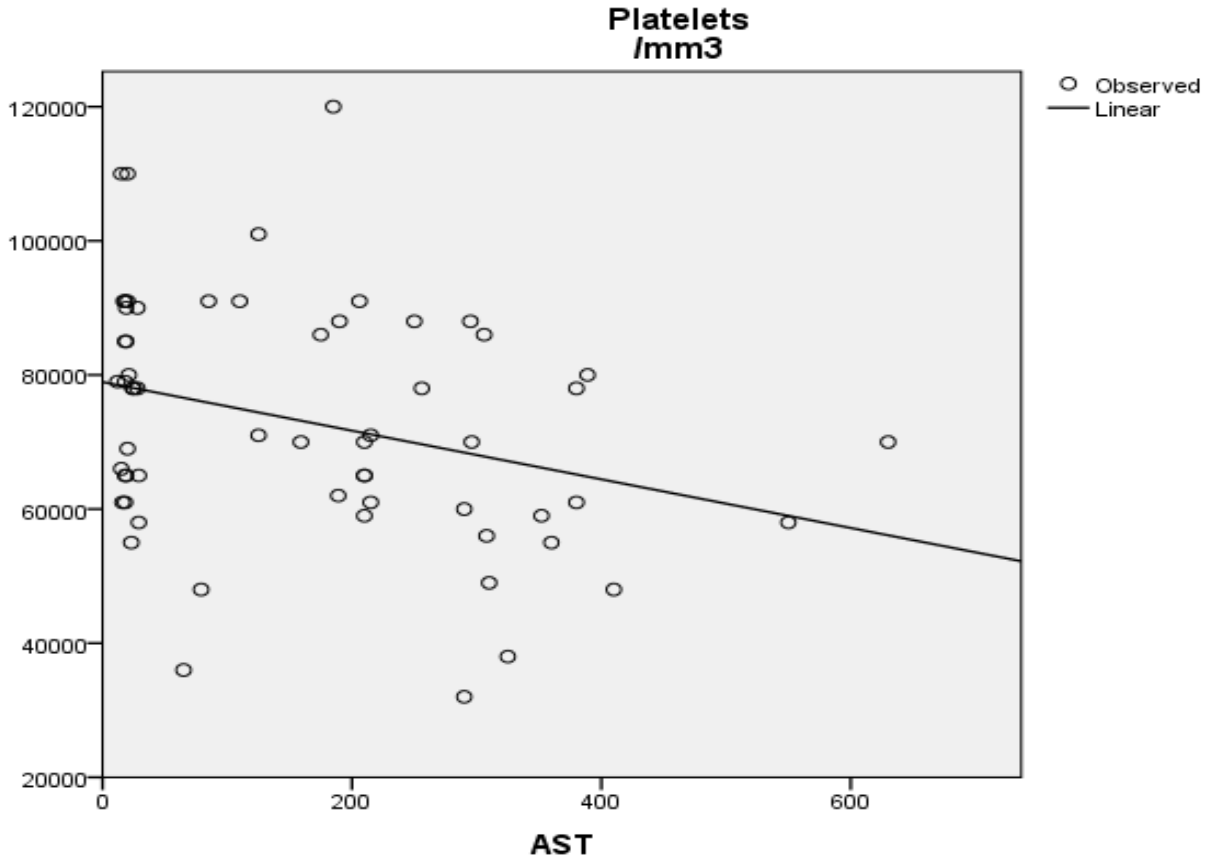


TABLE 11 : CORRELATION BETWEEN AST LEVELS AND MEAN ARTERIAL PRESSURE

		AST	MABP
AST	Pearson Correlation	1	-.593**
	Sig. (2-tailed)		.000
	N	60	60
MABP	Pearson Correlation	-.593**	1
	Sig. (2-tailed)	.000	
	N	60	60
**. Correlation is significant at the 0.01 level (2-tailed).			

There was a significant negative correlation between AST levels and mean arterial pressure count (r = -0.593). This implies that increase in AST levels is associated with decrease in platelets.

CORRELATION BETWEEN AST LEVELS AND MEAN ARTERIAL PRESSURE

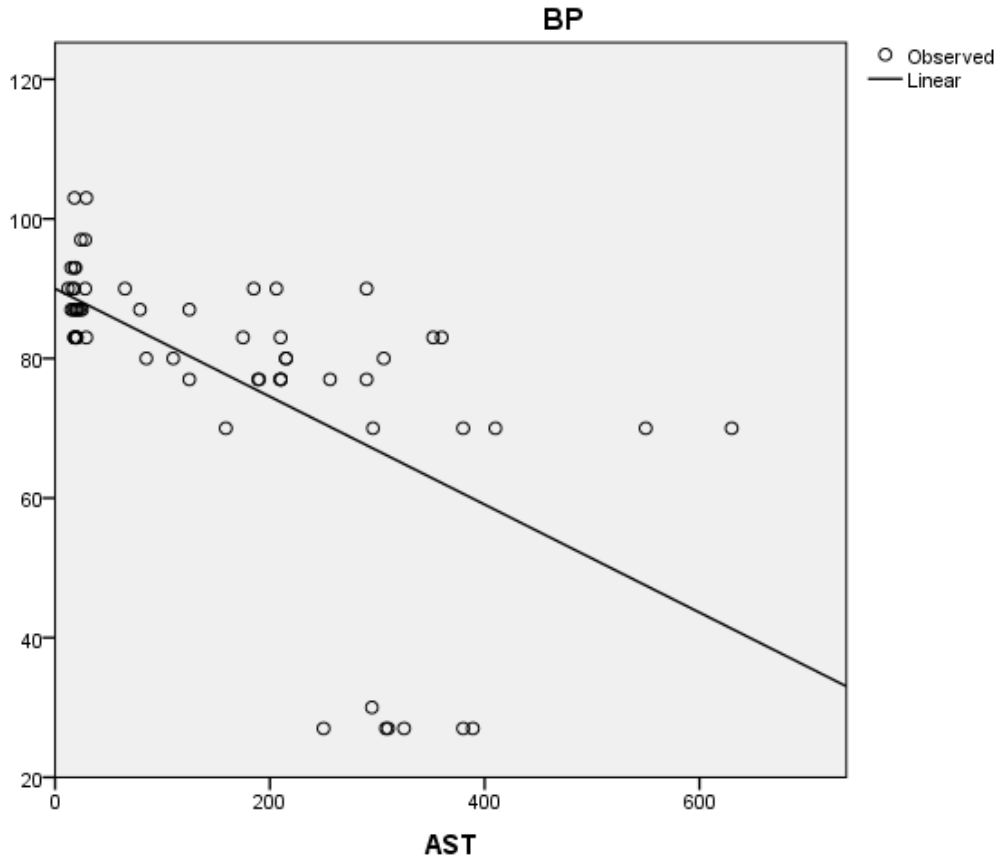


TABLE 12 : CORRELATION BETWEEN ALT AND PLATELETS

		ALT	Platelets /mm3
ALT	Pearson Correlation	1	-.324*
	Sig. (2-tailed)		.011
	N	60	60
Platelets /mm3	Pearson Correlation	-.324*	1
	Sig. (2-tailed)	.011	
	N	60	60
*. Correlation is significant at the 0.05 level (2-tailed).			

There was a significant correlation between ALT levels and Platelets count (r = -0.324). This implies that increase in ALT levels is associated with decrease in platelets.

CORRELATION BETWEEN ALT AND PLATELETS

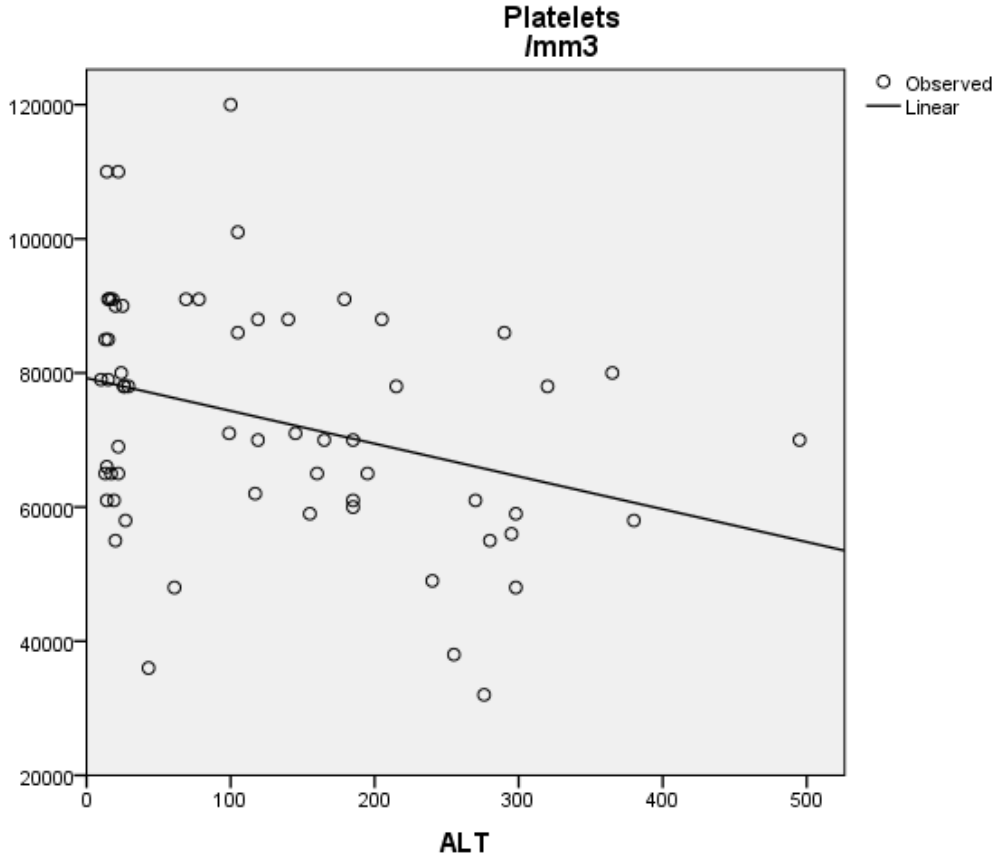


TABLE 13 : CORRELATION BETWEEN ALT AND MEAN ARTERIAL BLOOD PRESSURE

		ALT	MABP
ALT	Pearson Correlation	1	-.587**
	Sig. (2-tailed)		.000
	N	60	60
MABP	Pearson Correlation	-.587**	1
	Sig. (2-tailed)	.000	
	N	60	60

****. Correlation is significant at the 0.01 level (2-tailed).**

There was a significant correlation between ALT levels and mean arterial blood pressure (r = -0.587). This implies that increase in ALT levels is associated with decrease in mean arterial blood pressure.

CORRELATION BETWEEN ALT AND MEAN ARTERIAL BLOOD PRESSURE

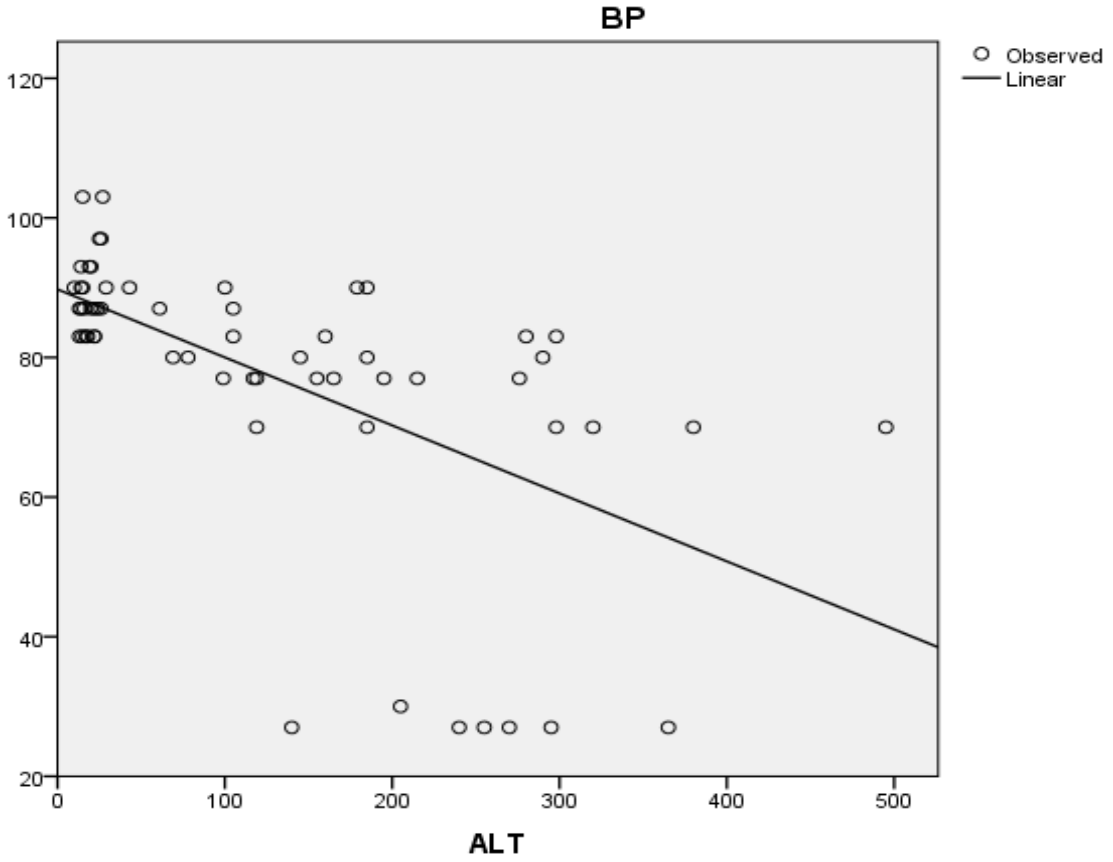


TABLE 14

SIGNIFANCE BETWEEN THROMBOCYTOPENIA AND BLEEDING TENDENCIES

		Thrombocytopenia		Total
		Yes	No	
Bleeding	Present	27	2	29
	Absent	29	2	31
Total		56	4	60

Chi square test was applied to test the significance between the thrombocytopenia and bleeding tendencies. There was no significant difference ($p = 0.945$) found between the variations in the thrombocytopenia and the bleeding tendencies. This implies that bleeding tendencies does not depends upon thrombocytopenia.

SIGNIFANCE BETWEEN THROMBOCYTOPENIA AND BLEEDING TENDENCIES

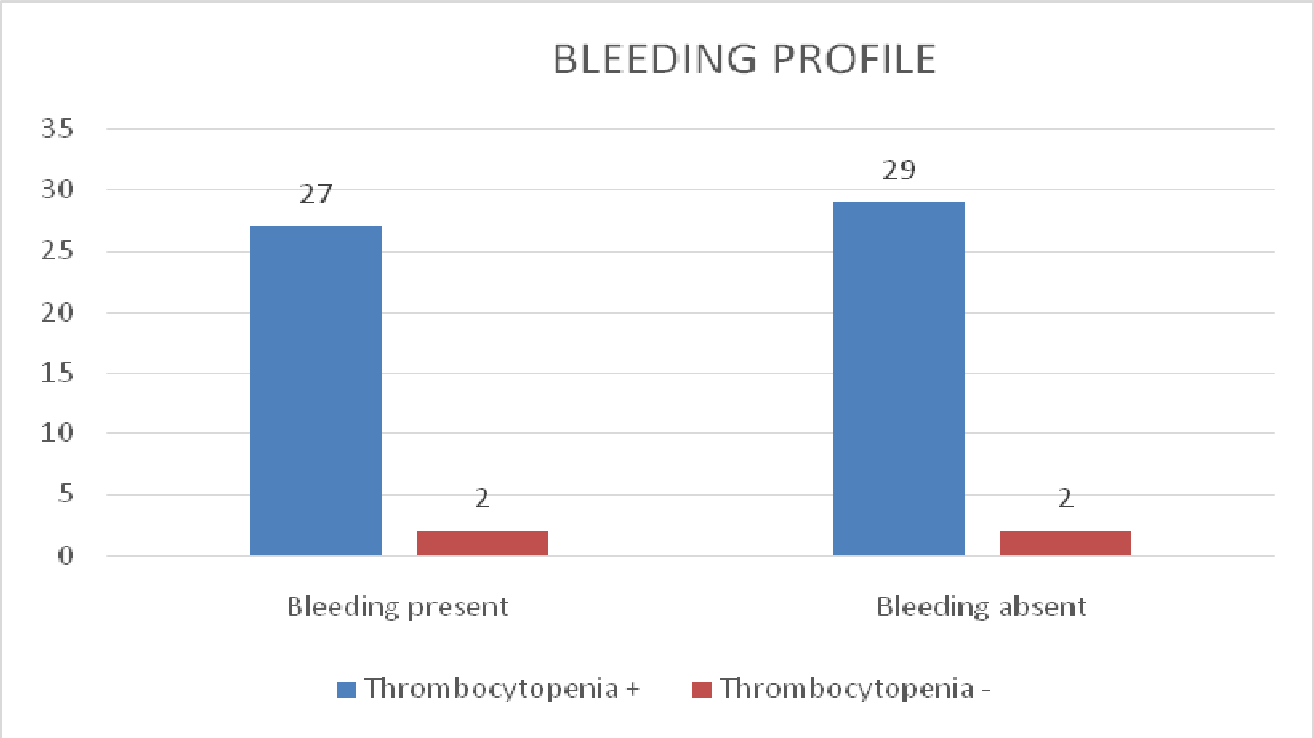
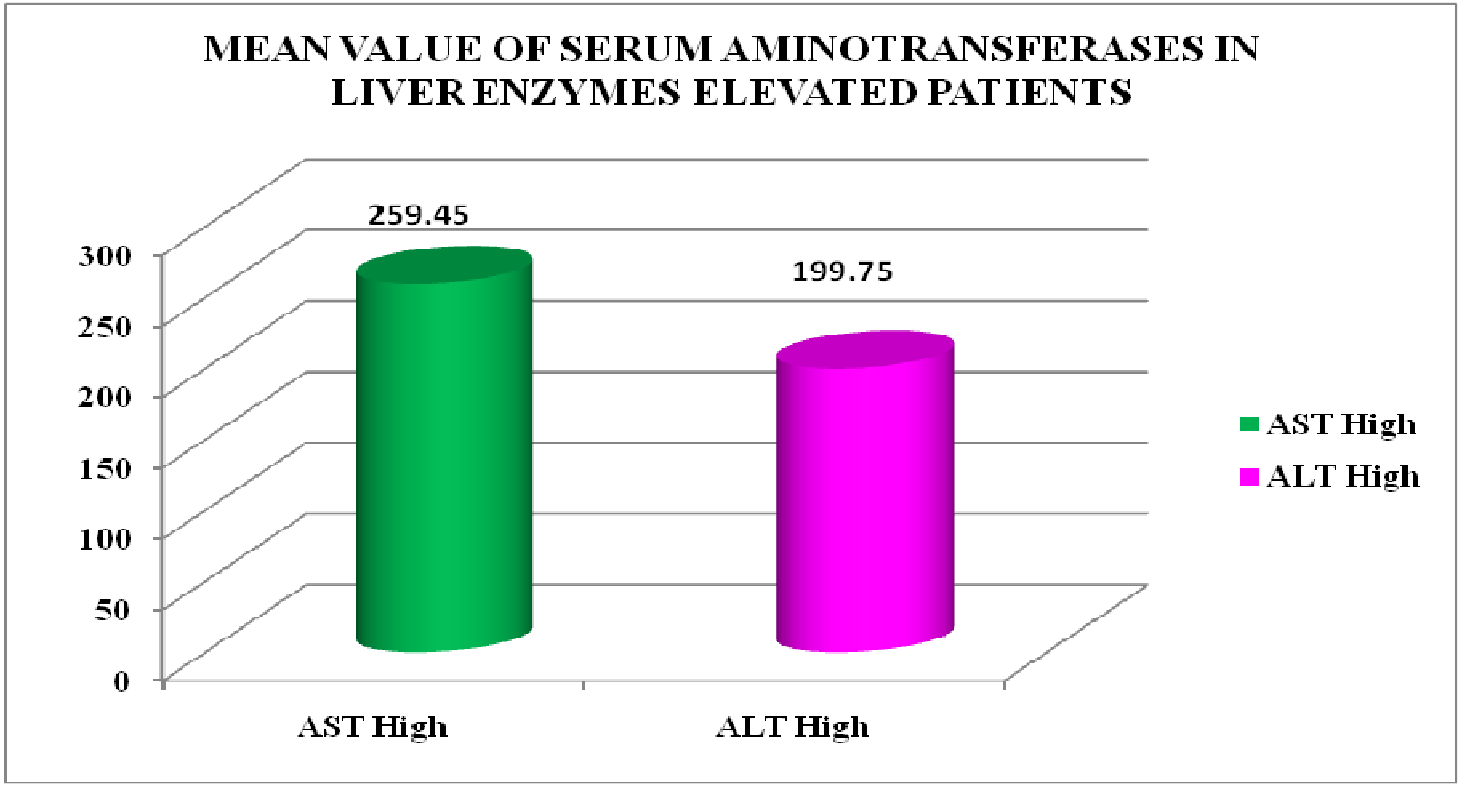


TABLE 15 : MEAN VALUE OF SERUM AMINOTRANSFERASES IN LIVER ENZYMES ELEVATED PATIENTS

Means	Value
AST High	**259.45**
ALT High	**199.75**

In our study, of those patients with elevated liver enzymes, AST was found to be higher than ALT levels.

MEAN VALUE OF SERUM AMINOTRANSFERASES IN LIVER ENZYMES ELEVATED PATIENTS



RESULTS

1. In this study, 60 patients of dengue IgM Elisa positive patients were studied.
2. Out of 60 patients, 32 were male and 28 were female.
3. Most of the patients were in the age group of 36 – 40 and none of them were below 18 years and above 55 years of age.
4. All the patients had fever as a presenting complaint. Most of them had myalgia at the time of presentation.
5. Six patients had hepatomegaly with or without spleenomegaly clinically.
6. Six patients presented with ARDS as a presenting feature. 19 patients had free fluid in USG abdomen. Bleeding tendencies were seen in 29 patients.
7. In our study, alcohol intake does not influence the levels of liver enzymes significantly.
8. Statistically, there was no significance between liver enzymes and age groups.
9. Elevated liver enzymes were found in 36 patients overall. Elevated liver enzymes were found in 29 patients with bleeding tendencies, 13 patient with shock, 6 patients with ARDS, 6 patients with hepatosplenomegaly and 19 patients with ascites in USG abdomen.

10. Of the liver enzymes, AST levels were significantly higher than ALT levels.
11. Thrombocytopenia was noted in 56 patients of which 27 had bleeding and 29 had no bleeding.
12. There was a negative correlation between levels of liver enzymes and platelet count.

DISCUSSION

Currently dengue is causing major public health concern throughout the World particularly in South East Asian countries. Recently dengue outbreaks caused significant morbidity and mortality in certain parts of Tamil Nadu mainly in Chennai, Tirunelveli and Madurai.

Hepatic dysfunction in dengue are common. It is due to either direct effect of virus on hepatocytes or due to reactive hepatitis. Hepatic involvement in dengue fever is in the form of elevated serum aminotransferase. Those patients with elevated liver enzymes are more likely to have increased risk of bleeding tendencies, shock, ARDS, renal failure and acalculous cholectystitis. In addition to decreased platelet count, hepatic dysfunction plays a significant role in bleeding. Hence, it is mandatory to evaluate serum aminotransferases in all patients with dengue fever.

It is found that, out of 60 patients, 36 patients had elevated liver enzymes and these patients had more complications like bleeding, shock, ARDS and hepatitis. Among the liver enzymes, AST levels are higher compared to the ALT levels.

Chen HC et al in 2004 found out that three tenth of patients with dengue had hepatic involvement. Hepatic involvement is significantly higher in Asian populations from 31.92%. They also found out that the rate of hepatic dysfunction in shock patients was somewhat higher than that of non shock patients.

Pancharoen et al found that mean values of AST and ALT were significantly increased in patients with DHF.

Kho CH et al reported that increased levels of AST and ALT are associated with severe bleeding manifestations in dengue patients.

In our study, out of 60 patients, 56 patients had thrombocytopenia. Out of 56 patients with thrombocytopenia, 27 patients were found to have bleeding tendencies and other 29 patients were found to have no bleeding, whereas out of 36 patients with elevated liver enzymes, 29 patients had bleeding tendencies.

Nguyen et al found that damaged liver function plays a significant role in bleeding in addition to thrombocytopenia.

Out of 60 patients, 13 patients were presented in shock. In all 13 patients liver enzymes were elevated with AST levels more than ALT levels.

Arun Sedhain et al study reported that AST and ALT levels were increased in DHF patients than DF significantly. They also found that AST levels were greater than ALT levels in contrast to viral hepatitis.

"Larreal Y et al reported jaundice in only two of 63 patients studied in their study known as hepatic alteration in dengue".

Arun Sedhain et al found that USG abdomen findings includes hepatomegaly. Gall bladder thickening and third space loss. They were higher significantly in DHF as compared to DF patients.

LIMITATION OF STUDY

1. Small sample size (60)
2. We did not check for dengue virus sub types.
3. Almost all the patients with dengue fever had thrombocytopenia. Thrombocytopenia was noticed in all patients with elevated liver enzymes.
4. Duration of study is six months only.
5. Antibody titres were not quantitated.

CONCLUSION

Hepatic involvement is common in dengue fever. It is characterized by elevated liver enzymes, AST more than ALT levels. Elevated liver enzymes are associated with complications like bleeding, shock and organ impairment. In addition to thrombocytopenia, hepatic involvement plays a significant role in bleeding. Elevated live enzymes have got prognostic value in this study. Hence, liver enzymes are mandatory in dengue fever to look for complications and it is of prognostic value. Those patients with elevated liver enzymes should be monitored carefully than those patients with normal liver enzymes.

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ABBREVIATIONS

DF	:	Dengue Fever
DHF	:	Dengue Haemorrhagic Fever
DSS	:	Dengue Shock Syndrome
AST	:	Aspartate Aminotransferase
ALT	:	Alanine Aminotransferase
MABP	:	Mean Arterial Blood Pressure
LFT	:	Liver Function Test
PT	:	Prothrombin time
APTT	:	Activated Partial Thromboplastin Time
FF	:	Free Fluid
ARDS	:	Acute Respiratory Distress Syndrome

PROFORMA

Name : IP No. :

Age/Sex : Patient ID No. :

History	
□ Fever	□ Bleeding tendencies
□ Joint pain	□ Oliguria
□ Headache	□ Alcoholism
□ Giddiness	□ Abdominal pain
□ Others	

Clinical Examination	
□ Pallor	□ Petechiae/purpura
□ Icterus	□ Bleeding gums
□ Pedal edema	□ Subconjunctival hemorrhage
□ Hepatomegaly	□ Splenomegaly

Vitals			
Temperatur		Pulse	
Respiratory rate		Blood pressure	

INVESTIGATIONS			
RFT		**LFT**	
Glucose	mg/dl	Total bilirubin	mg/dl
Urea	mg/dl	Direct bilirubin	mg/dl
Cratinine	mg/dl	ALP	U/l
Na^+	mEq/l	Total protein	g/dl
K^+	mEq/l	Albumin	g/dl
USG abdomen		Chest x-ray	

CBC		**Fever Workup**	
TC	mm^3	QBC for MP/Mf	
DC		MSAT for leptospirosis	
ESR	mm/hour	Blood culture	
Hemoglobin	g/dl	Widal test	
RBC count	$/mm^3$	Anti-HAV	
IgM Elisa for Dengue		HBsAg	
		Anti-HCV	

Parameter	Day 1	Day 3	Day 7
AST (U/l)			
ALT (U/l)			
Platelet count (/mm^3)			
Hematocrit (%)			

MASTER CHART

Sl.No.	Name	Age	Sex	History				Clinical Examination						
				Fever (Days)	Bleeding tendencies	Alcoholic History	Other symptoms	Pallor	Icterus	Bleeding signs	Hepatosplenomegaly	Chest X Ray	USG Abd.	IgM Dengue Elisa
1	Ganesan	35	M	10	-	Occasional	-	-	-	-	-	NAD	NAD	+ ve
2	Purushothaman	40	M	12	+	+	Joint pain	+	-	+	-	NAD	NAD	+ ve
4	Leya	38	F	8	-	-	+	+	-	-	-	ARDS	FF+	+ ve
4	Rajalakshmi	19	F	7	-	-	+	-	-	-	-	-	NAD	+ ve
5	Karpagam	28	F	8	+	-	+	+	-	+	-	-	-	+ ve
6	Mariammal	36	F	10	-	-	+	-	-	-	-	-	-	+ ve
7	Prabhakaran	27	M	12	+	+	+	-	-	+	+	-	FF+	+ ve
8	Balaji	31	M	13	+	+	+	-	-	+	-	-	-	+ ve
9	Kannan	46	M	7	+	+	-	-	-	-	-	-	-	+ ve
10	Murali	20	M	8	-	-	-	-	-	-	-	-	-	+ ve
11	Vinoth	19	M	9	-	-	+	-	-	-	-	-	-	+ ve

12	**Kumar**	**32**	**M**	**13**	+	+	-	-	-	-	-	-	**FF+**	**+ ve**
13	**Parvathy**	**19**	**F**	**12**	+	-	+	-	-	+	-	-	-	**+ ve**
14	**Shanmugapriya**	**20**	**F**	**10**	-	-	-	-	-	-	-	-	-	**+ ve**
15	**Shankari**	**39**	**F**	**210**	-	-	+	-	-	+	-	**NAD**	**NAD**	**+ ve**
16	**Rajesh**	**29**	**M**	**6**	-	-	+	-	-	-	-	**ARDS**	**FF**	**+ ve**

Sl.No.	Parameters										Parameters									
	Day 1										Day 3									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
1	90	130/80	14	99	38	0.9	0.9	90000	28	25	84	120/80	15	98.4	36	0.7	0.8	97000	26	22
2	105	90/60	15	101	44	1.0	0.8	78000	380	320	96	100/70	14	99.6	40	0.9	0.9	89000	300	260
4	120	90/60	36	102	46	1.0	1.1	58000	550	380	100	100/60	18	99	30	0.9	0.8	65000	390	170
4	116	80/?	16	98.8	40	0.6	0.8	88000	250	140	98	110/70	15	98.6	28	0.7	0.7	94000	280	120
5	90	110/70	15	101	28	0.7	0.6	65000	210	160	84	110/80	14	99.2	30	0.8	0.8	80000	170	100
6	84	120/70	14	98.8	24	0.6	0.6	110000	20	22	79	110/70	13	98.4	26	0.7	0.7	140000	22	18
7	98	110/70	13	102	36	0.9	0.7	55000	360	280	88	120/80	14	99.7	30	0.8	0.9	78000	270	175
8	96	110/80	13	100	30	0.6	0.9	60000	290	185	82	120/70	13	98.9	32	0.7	0.8	85000	150	80
9	94	130/70	13	102	28	0.5	0.8	120000	185	100	88	120/80	16	100	30	0.8	0.9	130000	145	65

10	**88**	**110/70**	**12**	**99.2**	**24**	**0.7**	**0.6**	**65000**	**29**	**22**	**80**	**110/80**	**13**	**98.7**	**32**	**0.6**	**0.7**	**78600**	**26**	**24**
11	**80**	**100/80**	**13**	**99.7**	**26**	**0.8**	**0.8**	**55000**	**23**	**20**	**76**	**120/70**	**12**	**99.4**	**30**	**0.9**	**0.9**	**70000**	**20**	**18**
12	**94**	**100/70**	**14**	**99.5**	**28**	**0.9**	**0.9**	**91000**	**110**	**78**	**89**	**110/80**	**13**	**99.2**	**26**	**0.9**	**0.7**	**96000**	**79**	**48**
13	**98**	**110/80**	**13**	**102**	**38**	**0.8**	**1.0**	**36000**	**65**	**43**	**96**	**100/70**	**12**	**101**	**29**	**1.0**	**0.9**	**40000**	**55**	**41**
14	**90**	**130/70**	**12**	**98.6**	**30**	**0.7**	**0.7**	**91000**	**18**	**15**	**86**	**110/80**	**12**	**98.4**	**24**	**0.6**	**0.7**	**99000**	**20**	**21**
15	**110**	**80/?**	**17**	**99.9**	**39**	**1.0**	**0.9**	**61000**	**380**	**270**	**99**	**100/70**	**15**	**99**	**32**	**0.9**	**0.7**	**78000**	**306**	**196**
16	**104**	**90/60**	**27**	**99.7**	**41**	**1.1**	**1.0**	**70000**	**630**	**495**	**90**	**100/80**	**17**	**99.1**	**34**	**0.9**	**0.9**	**80000**	**410**	**315**

Sl.No.	Parameters									
	Day 7									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
1	80	120/70	13	98.3	28	0.6	0.8	110000	23	25
2	86	130/80	12	98.5	30	0.7	0.7	140000	160	100
4	82	130/90	12	98.2	32	0.8	0.7	99000	150	86
4	86	120/80	14	98.3	28	0.7	0.6	130000	120	68
5	80	110/70	13	98.4	26	0.6	0.7	96000	110	48
6	78	120/70	13	98.2	29	0.8	0.7	165000	20	16
7	80	120/70	15	98.8	22	0.6	0.6	98000	165	95
8	78	110/80	14	98.3	26	0.5	0.5	96000	95	65
9	76	120/70	13	98.7	22	0.9	0.7	148000	90	46
10	79	110/70	14	98.6	28	0.7	0.7	91000	26	20

11	**75**	**120/70**	**13**	**98.5**	**26**	**0.6**	**0.8**	**96000**	**18**	**16**
12	**76**	**120/80**	**12**	**98.7**	**29**	**0.7**	**0.7**	**115000**	**57**	**39**
13	**90**	**110/70**	**12**	**99.9**	**32**	**0.9**	**0.7**	**59000**	**45**	**32**
14	**84**	**120/80**	**11**	**98.6**	**30**	**0.8**	**0.8**	**145000**	**19**	**16**
15	**72**	**120/70**	**13**	**98.7**	**30**	**0.6**	**0.5**	**105000**	**190**	**110**
16	**80**	**120/80**	**12**	**98.8**	**32**	**0.9**	**0.7**	**99000**	**170**	**118**

Sl.No.	Name	Age	Sex	History				Clinical Examination						
				Fever (Days)	Bleeding tendencies	Alcoholic History	Other symptoms	Pallor	Icterus	Bleeding signs	Hepatosplenomegaly	Chest X Ray	USG Abd.	IgM Dengue Elisa
17	Deepa	20	F	8	-	-	+	-	-	-	-	-	-	+ ve
18	Puhalenthi	37	M	12	+	-	+	+	-	+	-	-	-	+ ve
19	Selvam	30	M	10	+	-	+	+	-	+	-	-	FF	+ ve
20	Venkatesh	23	M	8	-		-	-	-	-	-	-	-	+ ve
21	Muniyammal	55	F	7	+	-	+	+	-	+	-	-	-	+ ve
22	Muthupandiyan	49	M	13	-		-	-	-	-	-	ARDS	FF+	+ ve
23	Rajasekaran	39	M	11	-		+	+	-	+	-	-	-	+ ve
24	Aaseela Begum	23	F	10	-	-	+	-	-	-	-	-	-	+ ve
25	Ismayil	40	M	11	-		+	-	-	-	-	-	-	+ ve

26	**Kandhammar**	**51**	**F**	**12**	+	-	-	+	-	+	-	-	**FF+**	**+ ve**
27	**Suseela**	**43**	**F**	**6**	-	-	+	-	-	-	-	-	-	**+ ve**
28	**Muthamizh**	**32**	**F**	**8**	+	-	+	+	-	+	-	-	-	**+ ve**
29	**Saranya**	**20**	**F**	**9**	-	-	+	-	-	-	-	-	-	**+ ve**
30	**Shanmugam**	**46**	**M**	**13**	+	-	-	+	-	+	+	-	**FF**	**+ ve**
31	**Ashok**	**45**	**M**	**12**	-	+	+	-	-	+	+	**NAD**	**NAD**	**+ ve**
32	**Mani**	**31**	**M**	**10**	+	+	+	-	-	+	-	**NAD**	**FF+**	**+ ve**

Sl.No.	Parameters										Parameters									
	Day 1										Day 3									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
17	90	110/70	15	98.9	30	0.9	0.9	69000	20	22	86	110/80	14	98.6	28	0.7	0.8	89000	20	23
18	99	90/60	17	99.5	24	0.8	0.8	48000	410	298	90	100/70	15	98.9	24	0.9	0.9	59000	298	179
19	106	90/?	16	99.9	28	0.9	0.9	88000	295	205	98	100/80	14	99	26	0.8	0.8	98000	150	115
20	90	110/70	15	100	26	0.6	0.6	65000	18	13	89	110/70	13	98.7	25	0.7	0.9	70000	19	17
21	118	80/?	14	100	30	0.7	0.7	49000	310	240	95	100/70	14	99.2	29	0.6	0.7	58800	295	180
22	110	100/70	28	102	32	0.6	0.5	71000	215	145	98	100/80	20	99.1	30	0.7	0.5	89000	140	97
23	104	90/70	16	103	34	0.5	0.6	62000	189	117	91	110/70	13	99	31	0.8	0.7	79000	110	81
24	90	110/80	17	99.8	30	0.8	0.8	79000	12	10	79	110/80	12	98.9	26	0.7	0.9	87000	18	17
25	88	120/80	15	101	21	0.9	0.7	61000	18	19	86	110/80	11	98.7	27	0.8	0.7	82000	17	15

26	**101**	**90/70**	**14**	**102**	**29**	**0.7**	**0.8**	**70000**	**210**	**165**	**95**	**110/70**	**12**	**98.9**	**26**	**0.9**	**0.9**	**89000**	**155**	**99**
27	**90**	**120/80**	**13**	**103**	**36**	**0.6**	**0.9**	**110000**	**15**	**14**	**79**	**120/80**	**11**	**98.7**	**21**	**0.7**	**0.8**	**125000**	**16**	**17**
28	**99**	**110/80**	**19**	**101**	**35**	**0.5**	**0.9**	**91000**	**206**	**179**	**89**	**110/70**	**12**	**99.2**	**37**	**0.9**	**1.0**	**98000**	**149**	**101**
29	**90**	**110/70**	**15**	**100**	**46**	**1.5**	**0.6**	**86000**	**175**	**105**	**81**	**110/80**	**13**	**98.7**	**41**	**0.9**	**0.7**	**104000**	**105**	**73**
30	**95**	**120/70**	**17**	**99.9**	**32**	**0.6**	**0.9**	**48000**	**79**	**61**	**80**	**130/70**	**12**	**99**	**31**	**0.7**	**0.8**	**67000**	**61**	**43**
31	**102**	**110/70**	**15**	**99.9**	**30**	**0.9**	**0.6**	**59000**	**352**	**298**	**90**	**120/80**	**15**	**98.9**	**30**	**0.8**	**0.7**	**71000**	**278**	**196**
32	**108**	**90/60**	**18**	**101**	**32**	**1.0**	**1.0**	**70000**	**296**	**185**	**98**	**100/70**	**14**	**99.2**	**28**	**0.9**	**0.8**	**85000**	**147**	**87**

Sl.No.	Parameters									
	Day 7									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
17	88	120/70	13	98.7	30	0.7	0.9	110000	19	24
18	84	110/80	14	98.6	28	0.9	0.8	90000	117	81
19	88	110/70	14	98.7	31	0.7	0.9	110000	78	61
20	89	110/80	13	99.7	28	0.7	0.8	88000	17	16
21	81	120/70	12	99	31	0.6	0.7	91000	105	87
22	85	120/80	13	98.7	28	0.7	0.8	115000	65	41
23	79	130/80	12	98.8	26	0.9	0.8	97600	71	50
24	75	110/70	11	98.6	21	0.7	0.6	126000	21	20
25	80	120/70	13	98.5	20	0.8	0.8	110000	15	16
26	88	120/80	12	98.6	25	0.6	0.9	99300	88	49

27	**72**	**110/80**	**13**	**98.4**	**21**	**0.7**	**0.8**	**165000**	**17**	**16**
28	**74**	**100/70**	**12**	**98.3**	**26**	**0.8**	**0.9**	**118000**	**81**	**62**
29	**77**	**130/70**	**13**	**98.6**	**27**	**0.7**	**0.6**	**115000**	**80**	**52**
30	**71**	**110/80**	**12**	**98.5**	**28**	**0.6**	**0.5**	**92000**	**48**	**30**
31	**89**	**120/70**	**14**	**98.7**	**31**	**0.6**	**0.7**	**95000**	**145**	**110**
32	**86**	**130/70**	**13**	**98.6**	**30**	**0.9**	**0.8**	**97000**	**91**	**59**

Sl.No.	Name	Age	Sex	History				Clinical Examination						
				Fever (Days)	Bleeding tendencies	Alcoholic History	Other symptoms	Pallor	Icterus	Bleeding signs	Hepatosplenomegaly	Chest X Ray	USG Abd.	IgM Dengue Elisa
33	Divya	26	F	8	-	-	-	-	-	-	-	NAD	NAD	+ ve
34	Shanthi	46	F	6	-	-	+	-	-	-	-	-	-	+ ve
35	Geetha	29	F	7	-	-	+	-	-	+	-	-	FF+	+ ve
36	Bharath	26	M	9	-	+	-	-	-	-	-	-	-	+ ve
37	Manoj	22	M	10	-	-	-	-	-	-	-	-	-	+ ve
38	Henith Raj	26	M	12	-	-	-	-	-	+	-	-	-	+ ve
39	Vivek	39	M	10	+	-	+	-	-	+	-	-	FF+	+ ve
40	Selvi	42	F	9	-	-	+	+	-	+	+	-	FF+	+ ve
41	Aarthi	36	F	11	-	-	+	-	-	-	-	-	-	+ ve
42	Prabha	21	F	7	-	-	-	-	-	-	-	-	-	+ ve

43	**David**	**39**	**M**	**11**	+	+	+	-	-	+	-	-	**FF+**	**+ ve**
44	**Siva**	**46**	**M**	**10**	+	+	+	-	-	+	-	**ARDS**	**FF+**	**+ ve**
45	**Hema**	**36**	**F**	**12**	-	-	-	-	-	-	-	-	-	**+ ve**
46	**Preethi**	**38**	**F**	**9**	-	-	+	-	-	+	-	-	-	**+ ve**
47	**Kalpana**	**43**	**F**	**10**	-	-	+	-	-	-	-	-	-	**+ ve**
48	**Basker**	**50**	**M**	**12**	+	+	+	-	-	+	-	-	**FF+**	**+ ve**

Sl.No.	Parameters										Parameters									
	Day 1										Day 3									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
33	91	110/70	13	99	28	0.8	0.9	85000	18	15	82	110/80	13	98.9	30	0.8	0.9	96000	19	17
34	87	120/70	12	98.7	30	0.9	0.8	66000	15	14	80	120/70	12	98.4	31	0.7	0.8	79000	21	18
35	105	90/70	19	99.8	36	0.9	0.6	59000	210	155	94	100/80	13	98.9	32	0.7	0.8	75000	159	106
36	95	110/80	18	99.9	30	0.8	0.5	61000	16	14	89	110/70	17	99	28	0.6	0.7	77000	19	17
37	89	120/70	13	99.7	26	0.7	0.6	85000	19	13	80	110/80	13	98.9	24	0.7	0.9	98000	16	15
38	98	90/70	12	99.9	28	1.0	0.9	88000	190	119	90	110/70	12	99.7	26	0.9	0.8	99600	115	84
39	94	100/70	13	99	26	0.9	0.8	91000	85	69	88	110/70	12	98.9	28	0.9	0.7	101000	59	49
40	99	90/70	14	99.8	38	1.0	0.9	78000	256	215	92	100/80	13	99.2	36	0.9	0.9	87900	179	148
41	90	110/70	13	98.7	36	1.0	0.9	65000	19	17	84	110/70	14	98.6	30	0.8	0.7	78000	19	18
42	88	120/70	12	98.8	30	0.8	0.7	78000	25	26	82	110/80	13	98.5	30	0.7	0.7	89000	28	26

43	**116**	**80/?**	**19**	**102**	**38**	**1.0**	**0.9**	**38000**	**325**	**255**	**98**	**100/70**	**18**	**99**	**32**	**0.9**	**0.8**	**60000**	**215**	**156**
44	**122**	**90/70**	**36**	**101**	**36**	**0.9**	**0.8**	**32000**	**290**	**276**	**99**	**100/80**	**19**	**99.4**	**30**	**0.8**	**0.7**	**55000**	**204**	**186**
45	**78**	**130/80**	**15**	**102**	**30**	**0.8**	**0.8**	**78000**	**24**	**26**	**86**	**110/70**	**18**	**99.5**	**28**	**0.9**	**0.9**	**90000**	**22**	**27**
46	**95**	**120/70**	**18**	**98.7**	**31**	**0.7**	**0.5**	**101000**	**125**	**105**	**89**	**120/80**	**17**	**98.6**	**26**	**0.7**	**0.8**	**110000**	**79**	**63**
47	**88**	**120/70**	**16**	**98.9**	**28**	**0.9**	**0.7**	**91000**	**17**	**16**	**78**	**110/80**	**15**	**98.7**	**28**	**0.7**	**0.7**	**110000**	**25**	**26**
48	**106**	**90/70**	**15**	**98.8**	**32**	**0.8**	**0.9**	**71000**	**125**	**99**	**98**	**100/70**	**14**	**98.6**	**30**	**0.6**	**0.8**	**90000**	**98**	**79**

Sl.No.	Parameters									
	Day 7									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
33	76	110/80	12	98.5	28	0.7	0.7	120000	19	18
34	74	130/70	11	98.7	26	0.6	0.9	110000	18	16
35	79	110/80	12	98.6	30	0.7	0.9	98000	93	79
36	87	110/80	13	98.7	30	0.6	0.7	106000	19	17
37	78	110/70	12	98.6	28	0.7	0.6	110000	16	15
38	76	120/70	13	98.8	26	0.8	0.8	115000	72	59
39	79	110/80	12	98.7	27	0.8	0.8	115000	48	39
40	80	110/80	13	98.5	26	0.7	0.8	97900	106	72
41	76	110/80	12	98.4	30	0.7	0.8	102000	17	16
42	80	120/70	13	98.5	30	0.8	0.8	110000	25	28

43	**86**	**110/80**	**12**	**98.7**	**28**	**0.7**	**0.7**	**98000**	**116**	**89**
44	**84**	**110/70**	**13**	**98.9**	**24**	**0.9**	**0.8**	**91000**	**105**	**91**
45	**86**	**110/80**	**12**	**98.6**	**26**	**0.7**	**0.7**	**110000**	**25**	**24**
46	**88**	**120/70**	**13**	**98.7**	**25**	**0.8**	**0.8**	**135000**	**55**	**49**
47	**76**	**120/70**	**15**	**98.5**	**28**	**0.6**	**0.7**	**125000**	**24**	**23**
48	**88**	**120/80**	**14**	**98.4**	**26**	**0.7**	**0.7**	**110000**	**71**	**52**

Sl.No.	Name	Age	Sex	History				Clinical Examination						
				Fever (Days)	Bleeding tendencies	Alcoholic History	Other symptoms	Pallor	Icterus	Bleeding signs	Hepatosplenomegaly	Chest X Ray	USG Abd.	IgM Dengue Elisa
49	Sivakumar	38	M	9	-	+	-	-	-	-	-	-	-	+ ve
50	Ilanchezhian	44	M	6	-	+	-	-	-	+	-	-	FF+	+ ve
51	Pushpavalli	55	F	11	-	-	+	-	-	-	-	-	-	+ ve
52	Ponnammal	43	F	10	-	-	+	-	-	+	+	ARDS	FF+	+ ve
53	Vasantha	38	F	8	+	-	+	-	-	-	-	-	-	+ ve
54	Nagammal	39	F	7	-	-	-	-	-	-	-	-	-	+ ve
55	Suresh	40	M	6	+	+	+	-	-	+	+	-	FF+	+ ve
56	Gopal	20	M	12	-	+	+	-	-	-	-	ARDS	-	+ ve
57	Raja	45	M	13	-	-	+	-	-	-	-	-	-	+ ve
58	Radhakrishnan	50	M	10	-	+	+	-	-	-	-	-	FF+	+ ve
59	Raghunathan	53	M	9	-	+	-	-	-	-	-	-	-	+ ve
60	Banu	36	F	8	-	-	+	-	-	-	-	-	-	+ ve

Sl.No.	Parameters										Parameters									
	Day 1										Day 3									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
49	89	120/80	14	99.4	30	0.7	0.6	90000	19	20	88	110/80	13	98.8	28	0.7	0.7	97000	22	24
50	104	80/?	19	99.9	28	1.0	0.5	56000	308	295	99	100/70	14	99	30	0.8	0.8	68000	199	119
51	92	120/70	15	98.9	26	0.7	0.7	80000	21	24	88	110/80	15	98.7	26	0.7	0.9	88800	24	27
52	106	100/70	38	99	28	1.0	1.0	86000	306	290	92	110/70	18	98.5	24	0.8	0.9	98000	221	145
53	105	90/60	18	98.9	24	0.6	0.6	70000	159	119	98	100/70	15	98.7	26	0.9	0.7	86000	101	69
54	88	130/90	15	98.6	30	0.4	0.5	58000	29	27	86	130/80	14	98.5	30	0.6	0.5	72000	27	26
55	118	80/?	19	99.9	32	0.9	0.8	80000	389	365	102	100/70	16	99	30	0.9	0.8	90000	257	215
56	102	100/70	32	99.8	36	0.8	0.7	61000	215	185	91	100/70	25	98.9	31	0.8	0.6	73000	145	116
57	88	130/90	15	101	24	0.5	0.5	79000	18	15	89	120/80	13	99.6	26	0.7	0.5	86000	21	23
58	106	90/70	13	99.6	29	0.9	0.7	65000	210	195	99	100/70	15	99.2	28	0.8	0.6	79000	136	105
59	88	130/70	12	99.8	30	0.8	0.7	78000	28	29	88	110/80	13	99.2	30	0.7	0.9	93000	30	33
60	84	110/70	13	98.7	24	0.7	0.5	91000	20	18	86	120/70	14	98.7	24	0.6	0.8	175000	20	17

Sl.No.	Parameters									
	Day 7									
	PR/mt	BP (mmHg)	RR/mt	Temp.°F	Urea (mg/dL)	Creatinine mg/dL	TB, DB mg/dL	Platelets /mm3	AST (IU/L)	ALT (IU/L)
49	86	130/70	13	98.6	27	0.6	0.6	125000	22	24
50	86	110/70	13	98.8	28	0.7	0.7	99000	96	78
51	84	120/80	12	98.4	26	0.8	0.8	110000	20	22
52	86	120/70	13	98.6	29	0.9	0.9	108000	98	67
53	84	120/80	12	98.4	39	0.8	0.8	99000	79	43
54	81	130/80	13	98.4	30	0.6	0.6	103000	22	19
55	89	110/70	12	98.7	28	0.7	0.7	106000	141	106
56	89	110/80	14	98.7	26	0.6	0.6	96000	79	61
57	86	120/80	13	98.9	24	0.7	0.7	105000	25	27
58	88	120/70	13	98.7	26	0.8	0.8	99000	86	73
59	86	120/70	12	98.9	28	0.7	0.7	115000	26	27
60	82	120/80	13	98.4	24	0.8	0.8	125000	28	26

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3
Telephone No : 044 25305301
Fax : 044 25363970
EC RegNo.ECR/270/Inst./TN/2013

CERTIFICATE OF APPROVAL

To
Dr.B.Govindarajan,
MD General Medicine PG,
Madras Medical College, Chennai-3.

Dear B.Govindarajan,

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Serum Aminotrans Ferase Levels in the Assessment of Severity of Dengue Fever" No.25062013.

The following members of Ethics Committee were present in the meeting held on 11.06.2013 conducted at Madras Medical College, Chennai -3.

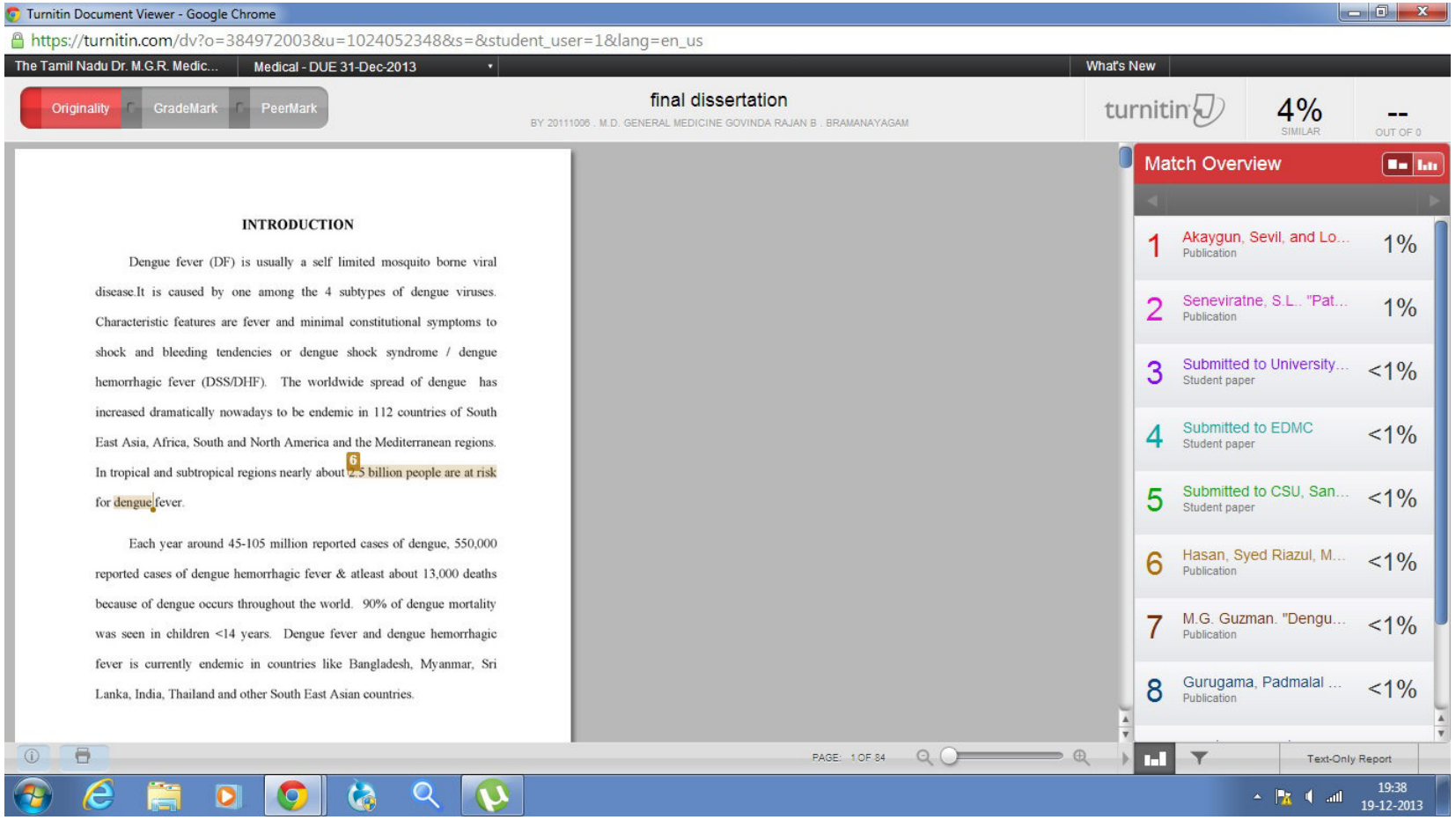
1. Dr.SivaKumar, MS FICS FAIS --- Chairperson
2. Prof. R. Nandhini MD -- Member Secretary
   Director, Instt. of Pharmacology ,MMC, Ch-3
3. Prof. Shyamraj MD -- Member
   Director i/c , Instt. of Biochemistry , MMC, Ch-3
4. Prof. P. Karkuzhali. MD -- Member
   Prof., Instt. of Pathology, MMC, Ch-3
5. Prof. A. Radhakrishnan MD -- Member
   Prof of Internal Medicine, MMC, Ch-3
6. Prof. S. Deivanayagam MS -- Member
   Prof of Surgery, MMC, Ch-3
7. Thiru. S. Govindsamy. BABL -- Lawyer
8. Tmt. Arnold Saulina MA MSW -- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

R Nandini 2/7/13
Member Secretary, Ethics Committee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INTRODUCTION
Dengue fever (DF) is usually a self limited mosquito borne viral disease.It is caused by one among the 4 subtypes of dengue viruses. Characteristic features are fever and minimal constitutional symptoms to shock and bleeding tendencies or dengue shock syndrome / dengue hemorrhagic fever (DSS/DHF). The worldwide spread of dengue has increased dramatically nowadays to be endemic in 112 countries of South East Asia, Africa, South and North America and the Mediterranean regions. In tropical and subtropical regions nearly about 2.5 billion people are at risk for dengue fever.
Each year around 45-105 million reported cases of dengue, 550,000 reported cases of dengue hemorrhagic fever & atleast about 13,000 deaths because of dengue occurs throughout the world. 90% of dengue mortality was seen in children <14 years. Dengue fever and dengue hemorrhagic fever is currently endemic in countries like Bangladesh, Myanmar, Sri Lanka, India, Thailand and other South East Asian countries.
Match Overview
1 Akaygun, Sevil, and Lo... Publication 1%
2 Seneviratne, S.L.. "Pat... Publication 1%
3 Submitted to University... Student paper <1%
4 Submitted to EDMC Student paper <1%
5 Submitted to CSU, San... Student paper <1%
6 Hasan, Syed Riazul, M... Publication <1%
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Submission time	19-Dec-2013 03:45PM
Total words	7193

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INTRODUCTION Dengue fever (DF) is usually a self limited mosquito borne viral disease.It is caused by one among the 4 subtypes of dengue viruses. Characteristic features are fever and minimal constitutional symptoms to shock and bleeding tendencies or dengue shock syndrome / dengue hemorrhagic fever (DSS/DHF). The worldwide spread of dengue has increased dramatically nowadays to be endemic in 112 countries of South East Asia, Africa, South and North America and the Mediterranean regions. In tropical and subtropical regions nearly about 2.5 billion people are at risk for dengue fever. Each year around 45-105 million reported cases of dengue, 550,000 reported cases of dengue hemorrhagic fever...

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